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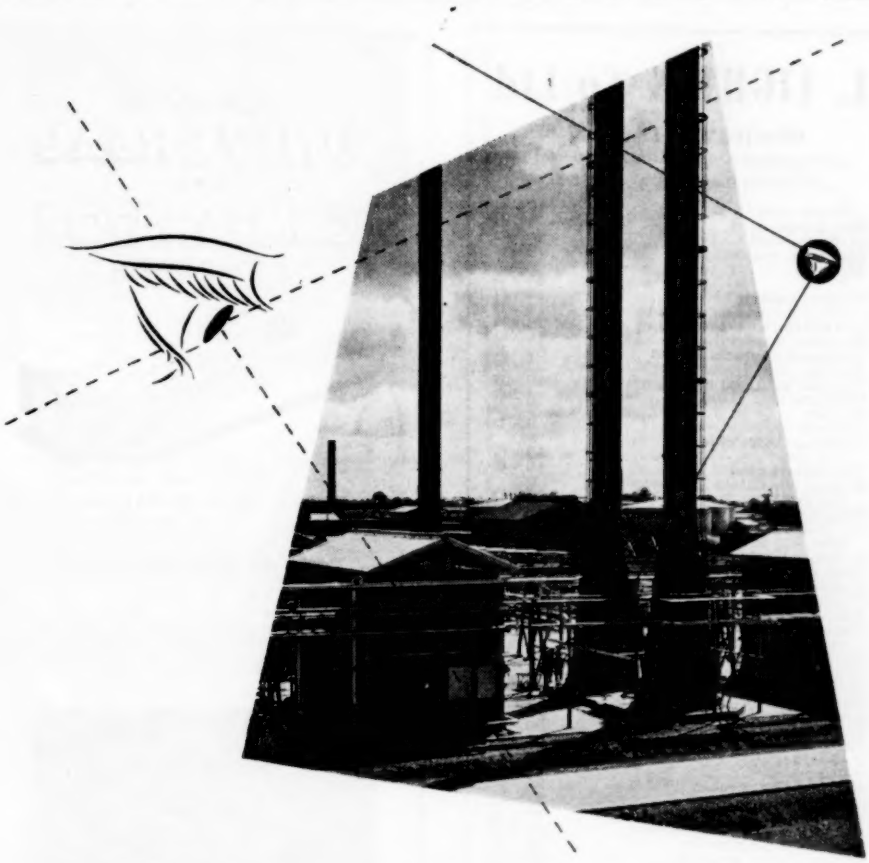

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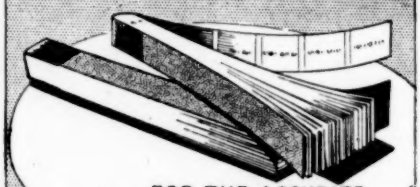

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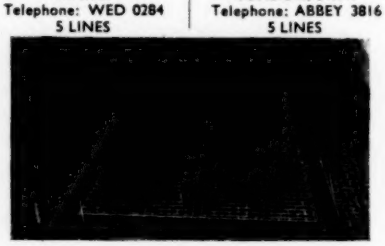

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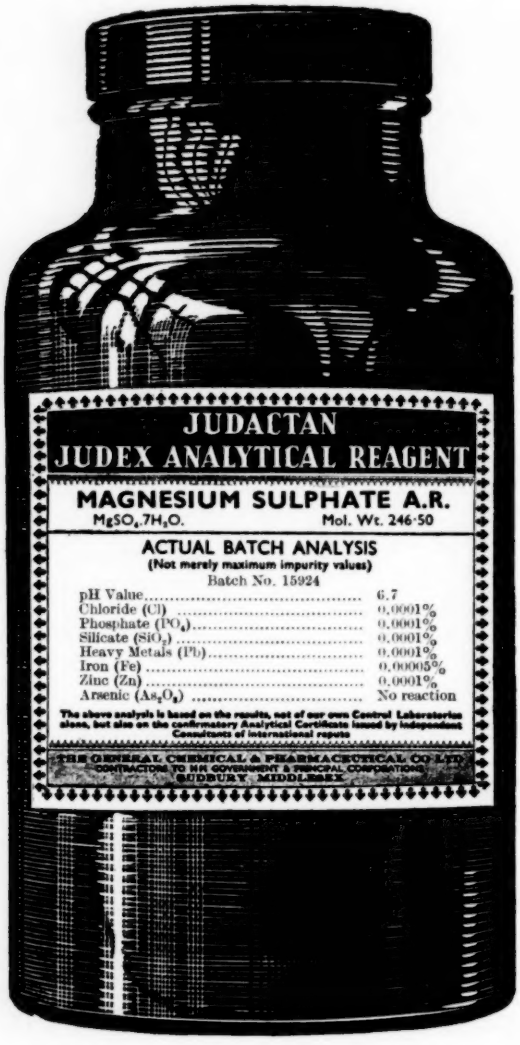
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217. *Hydrolytic Decomposition of Esters of Nitric Acid. Part I. General Experimental Techniques. Alkaline Hydrolysis and Neutral Solvolysis of Methyl, Ethyl,* iso*Propyl, and* tert.*-Butyl Nitrates in Aqueous Alcohol.*

By JOHN W. BAKER and (MRS.) D. M. EASTY.

Hydrolytic decomposition of organic nitrates, $CH_2R{\cdot}CH_2{\cdot}O{\cdot}NO_2$, involves the possibility of the occurrence of three simultaneous reactions : nucleophilic substitution (S_N) to give the alcohol $CH_2R{\cdot}CH_2{\cdot}OH$ and nitrate, β-hydrogen elimination (E) to give olefin $CHR{:}CH_2$ and nitrate, and α-hydrogen elimination (E_{CO}) to yield a carbonyl compound $CH_2R{\cdot}CHO$ and nitrite.

Hydrolysis of primary and secondary alkyl nitrates occurs at approx. one-fortieth of the rate of that of the corresponding alkyl bromides, thus making glass reaction vessels unsuitable (owing to alkali attack) ; it has been studied by using " Polythene " or " Fluon " vessels.

Kinetic studies of alkaline hydrolysis and neutral solvolysis of methyl, ethyl, *iso*propyl, and *tert.*-butyl nitrates in aqueous alcohol yielded the separate rate constants for each of the three concomitant reactions, at several tempertures. In 90% alcohol, alkaline hydrolysis of methyl nitrate results only in substitution (S_N2), the amount of nitrite formed being only just detectable, but both $E2$ and $E_{CO}2$ reactions occur (~2% each) with ethyl nitrate and become more important (~10% each) in *iso*propyl nitrate, whilst a considerable increase in olefin formation is observed from *tert.*-butyl nitrate, the ratio $100E1/(S_N1 + E1)$ increasing slightly with rise of reaction temperature. For methyl, ethyl, and *iso*propyl nitrates the total reactions ($S_N2 + E2 + E_{CO}2$) are of first order with respect to both [OH^-] and [RNO_3], and the rates are approximately in the ratios 70 : 7 : 1, the corresponding values of the Arrhenius energies of activation being 18·8, 23·6, and 26·3 kcal./mole, respectively. Hydrolysis of *tert.*-butyl nitrate is very much faster, is of first order, and is not markedly accelerated by hydroxyl ions, particularly in the more highly ionising solvent, 60% alcohol. In this solvent, moreover, the S_N2 reaction accounts for ≮99% of the total reaction with *iso*propyl nitrate, which is faster than that of ethyl nitrate.

In neutral solvolysis neither olefin- nor carbonyl-elimination reactions could be detected with methyl, ethyl, or *iso*propyl nitrates, the reaction rates being in the order Me > Et < Pr^i, but considerable first-order olefin elimination occurs with *tert.*-butyl nitrate, the ratio $100E1/(S_N1 + E1)$ being larger in alkaline media than in neutral solvolysis, and in 90% than in 60% alcohol.

The rates of alkaline hydrolysis of methyl and ethyl nitrates in 60% alcohol are smaller than in 90% alcohol, but that of *iso*propyl nitrate is greater, and that of *tert.*-butyl nitrate very much greater, in the more highly ionising solvent. Neutral solvolysis of methyl, ethyl, and *iso*propyl nitrates occurs faster, and that of *tert.*-butyl nitrate very much faster, in 60% than in 90% alcohol.

The significance and interpretation of the results are discussed in Part II (following paper).

VERY little systematic work on the mechanism of the hydrolytic decomposition of organic nitrates has been reported. Most of the early work (cf. Beilstein, " Handbuch, etc.," Vol. I, pp. 464, 515; Suppl. Vol. I, p. 273) was concerned with explosives, such as glycerol trinitrate and glycol dinitrate, which, because of their polyfunctional character and consequent kinetic complexity, are very unsuitable for the initial stages of the study of mechanism. The only certain conclusion which can be drawn from this early work is that alkaline hydrolysis of such nitrates involves a much more complex decomposition than simple fission into alcohol and metallic nitrate, the presence of nitrite, carbonyl derivatives, and organic acids having been detected in the products. In a paper which summarises and discusses these early results R. C. Farmer (*J.*, 1920, **117**, 806) claimed to have shown that

the primary reaction is a true hydrolysis of the general type $RNO_3 + H_2O \longrightarrow ROH + HNO_3$, followed by subsequent oxidation of the products, such as the alcohol, by nitric acid; he claimed that such secondary reactions could be suppressed either by reducing agents or by "protection" of the glycerol formed (by continuous extraction as its phosphoric ester). It was generally observed that the velocity of alkaline hydrolysis is 480 times greater than that of acid hydrolysis and, moreover, that formation of nitrite and the corresponding alcohol "oxidation" products is more prevalent in such alkaline media ("Organic Chemistry of Nitrogen," Sidgwick, Wilson Baker, and Taylor, 1937, Clarendon Press, Oxford, p. 8). Under such conditions the oxidising agent must, of necessity, be either the nitrate *anion* or the parent nitrate ester. It has now been shown that no oxidation of aqueous ethyl alcohol solutions by potassium nitrate occurs under the conditions of hydrolysis of nitrate esters used by us, although the formation of carbonyl derivatives and nitrite is confirmed. The exceedingly slow solvolytic reactions in aqueous alcohol (which we have also investigated) render oxidation by the nitrate ester very improbable; hence earlier views regarding the mechanism of such secondary reactions can scarcely be valid.

The direct formation of nitrite as a primary reaction product was envisaged in the (now discarded) view of Klason and Carlson (*Ber.*, 1906, **39**, 2752) that the initial reaction resulted in the formation of an alkyl peroxide:

$$RO{\cdot}O{\cdot}NO + KOH \longrightarrow RO{\cdot}OH + KO{\cdot}NO$$

followed, in the presence of a thiol, by the reaction

$$RO{\cdot}OH + 2RSH \longrightarrow ROH + R_2S_2 + H_2O$$

and they were thus able to isolate the alcohols glycerol and cellulose from technical "nitroglycerine" and "nitrocellulose," respectively.

A more recent investigation of the hydrolysis of *tert.*-butyl and benzyl nitrates by Lucas and Hammett (*J. Amer. Chem. Soc.*, 1942, **64**, 1928) revealed the concomitant formation of *iso*butene in the first-order solvolysis of the former:

$$\begin{cases} Bu^tO{\cdot}NO_2 + 2H_2O \longrightarrow Bu^tOH + H_3O^+ + NO_3^- \\ Bu^tO{\cdot}NO_2 + H_2O \longrightarrow C_4H_8 + H_3O^+ + NO_3^- \end{cases}$$

and of benzaldehyde, it was claimed, *both* in the first-order reactions * (*a*) and in the second-order reactions (*b*) in the case of the latter:

$$(a)\ \begin{cases} Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2 + 2H_2O \longrightarrow Ph{\cdot}CH_2{\cdot}OH + H_3O^+ + NO_3^- \\ Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2 \xrightarrow{H_2O} Ph{\cdot}CHO + HNO_2 \end{cases}$$

$$(b)\ \begin{cases} Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2 + OH^- \longrightarrow Ph{\cdot}CH_2{\cdot}OH + NO_3^- \\ Ph{\cdot}CH_2{\cdot}O{\cdot}NO_2 + OH^- \longrightarrow Ph{\cdot}CHO + H_2O + NO_2^- \end{cases}$$

These reactions were followed (in aqueous dioxan) by acid–alkali titration and determination of *iso*butene and benzaldehyde by standard methods.

It was therefore decided to commence a systematic kinetic study of the hydrolysis of organic esters of nitric acid, beginning with the simple alkyl mononitrates with which there should be a reasonable prospect of disentangling possibly superimposed modes of decomposition and of elucidating their detailed mechanisms. As a theoretical background there was available the considerable knowledge of the hydrolysis and solvolysis of alkyl halides and the concomitant elimination reactions resulting from the researches of Ingold, Hughes, and their collaborators. In view of the general applicability of such mechanisms to the hydrolytic and solvolytic decomposition of alkyl halides, onium compounds, etc., it seemed *a priori* that the hydrolysis of organic nitrates might partake of the same general

* Investigations at present in hand have revealed that neither nitrite nor benzaldehyde is formed in the first-order *solvolysis* of benzyl nitrate, but the reaction giving rise to such products is important in the second-order *alkaline* hydrolysis of this nitrate.

character. In one respect, however, the nitric esters have more in common with carboxylic esters than with alkyl halides, *viz.*, that, just as mechanisms involving both alkyloxy, CO·O┼R, and acyloxy, CO┼OR, types of fission have been shown to function in the hydrolysis of carboxylic esters (Day and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686), so there is a possibility that both nitrate, ⩾C┼O·NO_2, and nitrite, ⩾C·O┼NO_2, fission may occur in the hydrolysis of nitric esters. Thus the hypothesis upon which the experimental investigation was planned was that hydrolytic fission of organic nitrates might involve concomitant substitution and elimination reactions with both nitrate and nitrite fission, in all of which duality of mechanism, uni- and bi-molecular, might enter and be controlled by essentially the same kind of structural and environmental factors as have been shown to operate in the corresponding reactions of alkyl halides. Expressed for simplicity only in terms of the bimolecular mechanisms (the corresponding unimolecular mechanisms will be obvious) for hydrolysis with hydroxyl ions * the following three modes of hydrolytic decomposition are expected (Baker and Easty, *Nature*, 1950, **166**, 156):

(I) Nucleophilic substitution (S_N2)

$$OH^- + CH_2R\cdot CH_2\cdot O\cdot NO_2 \longrightarrow R\cdot CH_2\cdot CH_2\cdot OH + NO_3^- \text{ (alcohol + nitrate)}$$

(II) β-Hydrogen elimination, olefin formation ($E2$)

$$OH^- + H\cdot CHR\cdot CH_2\cdot O\cdot NO_2 \longrightarrow H_2O + CHR{:}CH_2 + NO_3^- \text{ (olefin + nitrate)}$$

(III) α-Hydrogen elimination, carbonyl formation ($E_{CO}2$)

$$OH^- + H\cdot CH_2\cdot CHR\cdot O\cdot NO_2 \longrightarrow H_2O + CH_2R\cdot CHO + NO_2^- \text{ (carbonyl + nitrite)}$$

Reactions (I) and (II) give nitrate ion, and (III) gives nitrite ion. In order to sort out these three simultaneous reactions the course of the hydrolysis has been followed by independent determinations of the various products formed, *viz.*, (1) acid–alkali titration (for OH^- or H_3O^+) which gives the combined velocity for all three reactions; (2) determination of nitrate ion, which gives the overall velocity of reactions (I) and (II); (3) olefin determination, which permits the apportionment of the velocity coefficient for the reactions (I) + (II), obtained from the nitrate determinations, between the two separate reactions; (4) nitrite ion determination, which gives the velocity coefficient for reaction (III) and could be checked by (5) determination of the carbonyl derivative formed. Thus a check on the concomitant formation of each of the products may be obtained: *e.g.*, when all three reactions are structurally possible the amount of hydroxyl ion removed should be equivalent at every stage of the reaction to that of nitrate + nitrite ions formed, whilst the values for nitrite alone should be equivalent to that obtained for the carbonyl derivative. Reaction (II) is structurally impossible with methyl nitrate, whilst reaction (III) is similarly excluded in the case of *tert.*-butyl nitrate. These features are especially significant since, if experiment confirms expectations, explanations of the formation of carbonyl compounds and nitrite based on secondary oxidation reactions are rendered extremely improbable.

Preliminary experiments soon revealed that alkaline hydrolysis of primary and secondary alkyl nitrates occurs very much more slowly than does that of the corresponding halides. Thus the value of 10^5k_2, the second-order velocity coefficient for the total reaction in the alkaline hydrolysis of ethyl nitrate in 90% ethyl alcohol (EtOH 90, H_2O 10% by vol.)

* The problems of acid-catalysed hydrolysis and attack by other nucleophilic reagents are under investigation.

at 59·3° is 4·44, whereas the corresponding value for ethyl bromide in 80% alcohol at 55° is 171 mole^{-1} l. sec.$^{-1}$ (Bateman, Cooper, Hughes and Ingold, *J.*, 1940, 931). The corresponding values of 10^5k_1 (sec.$^{-1}$) for solvolysis are: ethyl nitrate 0·003, ethyl bromide 0·139. This very slow hydrolysis introduced a formidable experimental difficulty. Experiments showed that the long periods over which it thus became necessary to study the reaction, even at relatively high temperatures (~60—100°), made glass reaction vessels unsuitable because of the extensive alkali attack. Attention was therefore first directed to the designing of suitable vessels in which the ordinary sealed glass bulb technique could be satisfactorily simulated. The reaction vessel evolved after much experiment was composed of " Polythene " (or " Fluon ") (see Fig. 1).

The reaction vessel itself consists of a " Polythene " lining vessel accurately turned from 1" rod, and of capacity 5·6 c.c. (to take a 5-c.c. sample of reaction mixture and allow for thermal expansion). The vessel is flanged and fits snugly into the cavity of a thick, cylindrical brass container, the purpose of which is to support the " Polythene " against deformation by pressure and thermal softening. The vessel is closed by an accurately plane-ground " Polythene " cap, a gas-tight joint being obtained by means of a screwed-in brass stopper-cap, in the base of which a second " Polythene " disc is fitted so that the actual pressure is applied between two " Polythene " surfaces and the flange of the reaction vessel. A small cylindrical hole in the base of the brass container permits the insertion of a thin metal rod by means of which the " Polythene " lining vessel can be carefully removed without disturbing its contents, which are then washed out for analysis. The vessel is conveniently suspended in the thermostat by means of a stout wire support which fits round the brass container below the cap flange. A series of such vessels is used for each kinetic experiment, each vessel corresponding to a single sealed bulb. Such " Polythene " vessels were found to be sufficiently resistant to alkali attack and were satisfactory for long periods up to 60°, but at higher temperatures cracking and deformation of the " Polythene " vessels occurred. Subsequently it was found that " Fluon " was an even more suitable polymer to employ for the lining vessels.* In this material the alkaline reaction mixture remains almost colourless (in " Polythene " it becomes somewhat brown) and alkali attack, even after repeated use, is undetectable. The coefficients of expansion of brass and both " Polythene " and " Fluon " are such that, whilst the lining vessel is easily removed after the whole vessel has been cooled in ice, warming to reaction temperatures causes expansion of the polymer relative to the brass and a tight fit is thus attained. The general agreement between the values of the velocity coefficients derived from titration of excess alkali with acid and from the gravimetric determinations of nitrate ion (when no $E_{CO}2$ reaction occurs) confirms the reliability of the alkali determinations in such vessels.

The techniques for determination of nitrate, nitrite, and olefin are described in the experimental portion.

No suitable method for the direct determination of the very small amounts of carbonyl derivatives formed in the hydrolysis of simple alkyl nitrates has yet been found. The 2 : 4-dinitrophenylhydrazones, although suitable for qualitative detection, are too soluble to be employed for gravimetric determination. In (unpublished) experiments with benzyl nitrates, however, this method (Eitel and Lock, *Monatsh.*, 1939, **72**, 385) is suitable and accurate for the determination of substituted benzaldehydes and the good agreement between the values for such aldehyde determinations and those of concomitantly formed nitrite ion justify the use of the latter determinations in order to evaluate the proportion of $E_{CO}2$ reaction in the aliphatic series.

In solvolysis experiments the reaction was carried out in sealed glass bulbs in the presence of accurately weighed amounts of pure calcium carbonate, such that there was always a slight excess over the amount of acid formed at various time intervals. By this means it was hoped to eliminate, or at least minimise, any possible autocatalysis by free nitric acid.

Since one criterion of mechanism is the effect on reaction rate of change in the ionising power of the solvent by application of the Hughes–Ingold theory (*J.*, 1935, 244), a solvent

* The difficulty in supply of suitable " Fluon " rod long prevented the general replacement of the " Polythene " vessels by this material, only a single sample vessel being available. Hence most of the investigations described in this paper were carried out in " Polythene," but " Fluon " is being used in our later work.

miscible with water was desirable. Initially aqueous dioxan, the solvent used by Lucas and Hammett (*loc. cit.*), was examined, but it was found that dioxan interfered with the accuracy of the gravimetric nitrate determinations with nitron. Since preliminary trials had shown that potassium nitrate, with or without addition of potassium hydroxide, had no action on aqueous ethyl alcohol under any of the conditions likely to be used in the kinetic experiments, it was decided to use this solvent. This makes possible direct comparison of our results with those for alkyl halides, which were obtained in the same type of solvent. It was also proved that when the standard ether-extraction technique is used for removal of unchanged alkyl nitrate, no interference with the gravimetric determination of nitrate ion in the aqueous solution is encountered. A further advantage is that, since preliminary examination suggested that even free nitric acid (~0·03M) has no detectable reaction with aqueous alcohol for periods up to ~168 hours at 60°, it should be possible to obtain at least initial rates in the same solvent when acid catalysis of hydrolysis is investigated.

This communication describes the results of investigations with methyl, ethyl, *iso*-propyl, and *tert.*-butyl nitrates, aimed at providing a general picture of the field into which

FIG. 1.

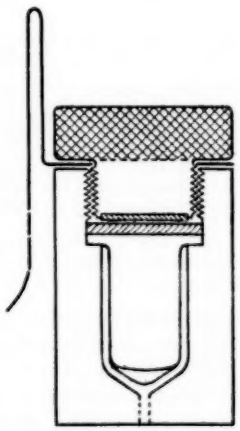


FIG. 2.

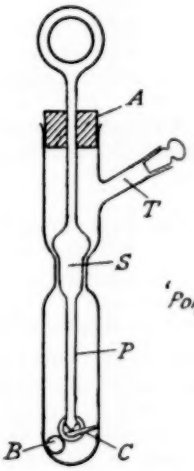
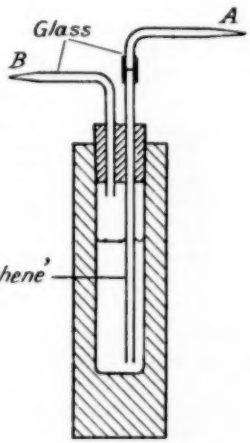


FIG. 3.



the finer details, such as salt effects, etc., can later be fitted. A general discussion of the results is given in Part II (following paper).

Methyl and Ethyl Nitrates.—Examination of methyl nitrate presented some unexpected difficulties. 90% Alcohol which was as little as 0·03M with respect to both nitrate and potassium hydroxide immediately became turbid, the separated droplets being essentially a concentrated aqueous solution of potassium hydroxide. The reason for such non-homogeneity, which does not occur with any of the other alkyl nitrates studied, is not known. To overcome this difficulty kinetic investigations with this nitrate were conducted in 75% and 60% alcohol, in both of which solvents homogeneity could be maintained.

Since the parallel and equivalent formation of nitrate ions with the loss of hydroxyl ion (nitrite formation is negligible with methyl nitrate) is an essential feature of the postulated mechanisms, typical data which unequivocally demonstrate such equivalence are recorded in Table 1. Incidentally, the great improvement in individual consistency which is obtained in " Fluon " vessels relative to the " Polythene " vessels first employed is apparent. With the gradual replacement of " Polythene " by " Fluon " it thus became unnecessary to determine hydroxyl ion, nitrate, and nitrite for every individual sample.

In all Tables x is the amount of reaction which has occurred at time t.

TABLE 1. (i) *Neutral solvolysis of methyl nitrate in* 60% EtOH *at* 60·2° (" *Monax* " *glass bulbs*).

Initial $[CH_3NO_3] = 0{\cdot}0301$M.

Time (hours)	10^2x (mole l.$^{-1}$) H_3O^+	10^2x (mole l.$^{-1}$) NO_3^-	10^7k_1 (sec.$^{-1}$) * H_3O^+	10^7k_1 (sec.$^{-1}$) * NO_3^-
336	—	0·65	—	2·03
450	—	0·83	—	2·00
617	0·972	—	1·75	—
953	1·42	1·49	1·86	1·99
1698	2·02	2·08	1·82	1·92
			Mean 1·81 ± 0·04	1·99 ± 0·03

(ii) *Alkaline hydrolysis of* $EtNO_3$.

Time (hours)	10^2x (mole l.$^{-1}$) OH^-	NO_3^-	NO_2^-	10^5k_2 (mole^{-1} l. sec.$^{-1}$) * OH^-	NO_3^-
(a) *In* 90% EtOH *at* 59·3° (" *Polythene* "). Initial $[EtNO_3] = 0{\cdot}0307$; $[KOH] = 0{\cdot}0999$M.					
4	0·172	0·196	—	4·05	4·60
18	$0{\cdot}709_5$	$0{\cdot}723_5$	—	4·21	4·31
24	0·858	0·898	—	3·97	4·15
30·42	1·035	1·063	—	3·98	4·10
44	1·428	1·328	—	4·30	4·00
∞ (816)	2·984	2·790	0·148	—	—
		2·938		Mean 4·11 ± 0·1	4·2 ± 0·2
(b) *In* 60% EtOH *at* 44·8° (" *Fluon* "). Initial $[EtNO_3] = 0{\cdot}309$; $[KOH] = 0{\cdot}0909$M.					
43·5	0·189	0·200	—	0·451	0·475
94·0	0·403	0·410	—	0·460	0·474
162·0	0·692	0·658	—	0·497	0·471
233·6	0·864	0·888	—	0·450	0·469
329·7	1·17	1·13	—	0·475	0·453
425·9	—	—	0·012	—	—
427·4	1·32	1·38	—	0·434	0·463
				Mean 0·46 ± 0·02	0·47 ± 0·01

* Values of k_1 and k_2 are uncorrected for expansion.

In the alkaline hydrolysis of methyl nitrate, contrary to statements in the literature, the reaction is essentially bimolecular *substitution* (S_N2) only, since nitrite produced was barely detectable (<0·1% of the total reaction). The results obtained are given in Table 2. In all such summarised results the values of the velocity coefficients have been corrected for solvent expansion from room temperature to the temperature of the experiment. The mean deviations from the mean value are recorded in each case.

TABLE 2. *Values of the second-order velocity coefficients for the alkaline hydrolysis* (S_N2) *of methyl nitrate in* 75% *and* 60% EtOH.

Initial $[MeNO_3] \sim 0{\cdot}03$; $[KOH] \sim 0{\cdot}09$M.

Solvent, Aq. EtOH (vol. %)	Temp.	10^5k_2 (mole^{-1} l. sec.$^{-1}$) (OH^-)	(NO_3^-)	Mean	E (kcal./mole)
75	60·2°	41·2 ± 1·6	39·2 ± 1·5	40·2 ± 1·5	18·8
,,	44·8	10·3 ± 0·25	9·92 ± 0·6	10·1 ± 0·4	
60	60·2	22·0 ± 0·5	22·3 ± 0·8	22·1 ± 0·7	19·7
,,	44·8	5·2 ± 0·2	5·2 ± 0·2	5·2 ± 0·2	

The slower alkaline hydrolysis of ethyl nitrate was more difficult to follow since, with this nitrate, the proportions of the two elimination reactions ($E2$ and $E_{CO}2$), although small, are significant, as the following analysis shows :

Solvent	Temp.	$100X/(S_N2 + E2 + E_{CO}2)$ $X = S_N2$	$E2$	$E_{CO}2$
90% EtOH	80°	94	4	2
,,	60	93·2	2	4·8
60% EtOH	60	98·8	0·2	1

Such olefin and nitrite determinations were therefore subject to rather large errors and are only approximate; for this reason no separate values of the Arrhenius energies of activation for $E2$ and $E_{CO}2$ are recorded but only those for the total reaction, for which a plot of log k_2 and $1/T$ gave a good straight line. The results are in Table 3.

TABLE 3. *Alkaline hydrolysis of ethyl nitrate under various conditions in aqueous alcohol.*

Initial [$EtNO_3$] ~0·03; [KOH] ~0·09M.

Solvent, Aq. EtOH (vol. %)	Temp.	10^5k_2 (mole^{-1} l. sec.$^{-1}$) S_N2	$E2$	$E_{CO}2$	Total	E (total reaction) (kcal./mole)
90	59·3°	4·13	0·08	0·21	4·44 ± 0·04	
90	45·0	(not determined)			0·98 ± 0·1	23·6
90	30·0	0·131	0·006	0·003	0·14 ± 0·017	
60	~84	(not determined)			~5·8	
60	60·2	2·34	0·004	0·024	2·37 ± 0·11	21·9
60	44·8	0·47	—	(0·004)	0·47 ± 0·012	

At this stage it may be noted that, for both methyl and ethyl nitrates, the velocity of alkaline hydrolysis is slower in the more highly ionising solvent, 60% alcohol. There is an indication that the incursion of the two elimination reactions (always small) is also less in this solvent than it is in 90% alcohol.

In view of the very much smaller nucleophilic power of the water or alcohol molecule compared with that of the hydroxyl ion it is not surprising that the neutral solvolyses of both ethyl and methyl nitrates are extremely slow reactions: the half-life period for ethyl nitrate in 90% alcohol at 60° is ~250 days. In these solvolytic reactions, substitution (S_N2) is the sole reaction and no elimination reactions could be detected. The values of the velocity coefficients for neutral solvolysis of methyl and ethyl nitrates are given in Table 4.

TABLE 4. *Values of the first-order velocity coefficients for neutral solvolysis of* RNO_3 *in aqueous aocohol.*

Initial [RNO_3] ~0·03M.

R	Solvent, Aq. EtOH (vol. %)	Temp.	Mean 10^5k_1 (sec.$^{-1}$)	E (kcal./mole)
CH_3	90	96·2°	0·28 ± 0·01$_5$	24·8
,,	,,	60·2	0·0073 ± 0·0007	
,,	60	97·7	0·87 ± 0·06	24·8
,,	,,	60·2	0·019$_6$ ± 0·001	
C_2H_5	90	59·3	0·003 ± 0·0003	
,,	60	60·2	0·011 ± 0·0008	

Attention may be called to two points. First, unlike the alkaline hydrolyses, the solvolytic reaction is *faster* in the more highly ionising solvent, the 60% alcohol. The velocity coefficient is, of course, of pseudo-first-order for a *bimolecular* reaction in which the solvent concentration is maintained effectively constant. It being assumed that both water and alcohol molecules are equally effective, the approximate total solvent concentration can be calculated to be 20·8 and 32·2 moles per l. respectively for 90 and 60% alcohol. On this basis the values for the second-order velocity coefficients for the solvolytic reaction at 60° are approximately as follows:

EtOH:	90%	60%	
$MeNO_3$	~3 × 10^{-9}	~6 × 10^{-9}	mole^{-1} l. sec.$^{-1}$
$EtNO_3$	~1·4 × 10^{-9}	~3 × 10^{-9}	,, ,,

Comparison with the corresponding values for hydrolysis by hydroxyl ion (Tables 2 and 3, using the value in 75% aqueous alcohol, the only one available, for comparison in the case of methyl nitrate) shows that the velocities with the much more strongly nucleophilic hydroxyl ion are greater by the order of 10^4 to 10^5.

iso*Propyl and* tert.*-Butyl Nitrates.*—Experimentally *iso*propyl nitrate was the most difficult of the nitrates to investigate since, in the less ionising solvent, its velocity of decomposition by alkali is much slower even than that of ethyl nitrate and, moreover, all three reactions, S_N2, $E2$, and $E_{CO}2$ occur in significant proportions. Hence simultaneous

determinations of hydroxyl ion, nitrate, nitrite, and olefin are essential. Because of these complications it has, so far, been studied only at two temperatures in 90% alcohol and at a single temperature in 60% alcohol. Most of the work was carried out in " Polythene " vessels and in these the values obtained from determinations of hydroxyl ion used were always rather higher (~10%) than those derived from determinations of nitrate + nitrite ions formed, and the infinity value somewhat exceeded that theoretically required for 100% hydrolysis. As " Fluon " vessels were introduced this disparity was greatly reduced or eliminated, and it may therefore be most probably ascribed to slight alkali attack on the " Polythene " vessels during the prolonged contact necessary to follow the reaction to completion. For this reason results have been calculated on the nitrate and nitrite values, which are regarded as the more reliable.

A summary of the results for the second-order velocity coefficients in alkaline, and for first-order velocity coefficients in neutral, hydrolysis is given in Table 5, all values being corrected for solvent expansion where necessary.

TABLE 5. *Hydrolysis of* iso*propyl nitrate in aqueous ethyl alcohol.*

Initial [Pr^iNO_3] ~0·03; [KOH] ~0·09M.

Solvent, Aq. EtOH (vol. %)	Temp.	(*a*) Alkaline hydrolysis 10^5k_2 (mole^{-1} l. sec.$^{-1}$) S_N2	$E2$	$E_{CO}2$	Total	(*b*) Neutral solvolysis 10^5k_1 (sec.$^{-1}$) S_N	E_{CO}	Total	Reaction proportions, % S_N2	$E2$	$E_{CO}2$
90	79·7°	5·3	0·72	0·55	6·52 (*a*)	—	—	—	80·4	11·1	8·5
,,	59·3	0·46	0·09	0·09	0·65 (*a*)	—	—	—	71·8	14·5	13·7
,,	75	—	—	—	—	0·038	*ca.* 0·0003	0·038	>99	0	<1
,,	60	—	—	—	—	0·007	0	0·007	100	0	0
60	60·2	2·98	0	0·03	3·01	—	—	—	99	0	1
,,	60·2	—	—	—	—	0·048	0	0·048	100	—	0

(*a*) These values give E for S_N2 = 27·9 and for total reaction = 26·3 kcals./mole.

The determinations of olefin and nitrite are again not regarded as sufficiently accurate to warrant separate evaluation of the values of the Arrhenius E values for the $E2$ and $E_{CO}2$ reactions. They are of the order of 20—23 kcal./mole. The formation of a carbonyl compound was qualitatively confirmed although it could not be determined quantitatively.

Attention may be directed to the points: (1) the proportion of total elimination reactions ($E2$ + $E_{CO}2$) which occurs with the nitrate is considerably less than that of olefin elimination from *iso*propyl bromide under comparable conditions (Hughes, Ingold, and Shapiro, *J.*, 1936, 225); (2) whilst in 90% alcohol the total velocity of alkaline hydrolysis of *iso*propyl nitrate is only about one-seventh of that of ethyl nitrate under the same experimental conditions, in 60% alcohol *iso*propyl nitrate is hydrolysed slightly *faster* than ethyl nitrate, and, moreover, in this solvent elimination reactions are reduced to negligible proportions.

In both solvents there are indications from the limited data available that the rate of neutral solvolysis of the *iso*propyl compound is greater than that of ethyl nitrate, and no appreciable elimination could be detected, substitution accounting for $\not<$99% of the total reaction.

For comparison, the approximate value of the second-order velocity coefficient for the solvolysis of *iso*propyl nitrate (calculated on the basis of solvent concentration) in 60% alcohol at 60° is ~1·5 × 10^{-8}, *i.e.*, ~10^{-3} times that for attack by hydroxyl ion under the same conditions.

More extensive examination of *tert.*-butyl nitrate has been possible because the hydrolytic reactions are sufficiently rapid to be conveniently studied at lower temperatures and in glass vessels. For alkaline hydrolysis the velocity coefficients calculated on the basis of a first-order law are reasonably constant throughout any one experiment, but Expts. Nos. 2 and 3 (Table 6) suggest that change in the initial hydroxyl-ion concentration has a small effect on the velocity. Olefin elimination is also important, both in alkaline hydrolysis and in netural solvolysis, but carbonyl elimination is, of course, structurally impossible. Analysis of the data for both alkaline hydrolysis and neutral solvolysis in 90% alcohol is given in Table 6.

In the presence of 2—4 molecular proportions of alkali the values of both $k_1(S_N1)$ and $k_1(E1)$ are somewhat higher than those for the solvolytic reaction at the same temperature (the disparity being greater in the elimination reaction). When, however, the initial concentration of alkali is only about one-fifth of the initial concentration of *tert.*-butyl nitrate (No. 3), the value of $10^5k_1(S_N1 + E1)$ (4·2) closely approximates to that (3·66) for the solvolytic reaction at the same temperature (No. 6) and, moreover, its value remains

TABLE 6. *Alkaline hydrolysis and neutral solvolysis of* tert.*-butyl nitrate in* 90% EtOH.

	Initial concn. (mole l.$^{-1}$)			10^5k_1 (sec.$^{-1}$)			E (kcal./mole)		Reaction proportions, %	
No.	[OH$^-$]	[Bu^{t}NO$_3$]	Temp.	S_N1	$E1$	Total	S_N1	$E1$	S_N1	$E1$
1	0·0877	0·0211	30°	18·5	5·5	24·0	22·3	25·4	77	23
2	0·0876	0·0420	20	4·9$_3$	1·5$_4$	6·4$_7$			76·2	23·8
3	0·0109	0·0486	20	—	—	4·2			—	—
4	0·0883	0·0437	0	0·32	0·06	0·38			84·4	15·6
5	0	0·0298	30	13·9	2·38	16·3	22·6	23·5	85·4	14·6
6	0	0·0245	20	3·10	0·56	3·66			84·8	15·2
7	0	0·0473	0	0·22	0·03$_3$	0·25 *			87·2	12·8

* Cf. $10^5k_1 = 0·26$ when 0·0463M-$NMe_4^+\}NO_3^-$ is added.

essentially constant as the medium changes from alkaline, through neutral, to acid as the reaction proceeds (cf. p. 1207). Addition of tetramethylammomium nitrate caused no detectable alteration in the value of k_1 (cf. No. 7), but this *may* arise from a fortuitous compensation between a velocity-increasing ionic-strength effect and a retarding mass-law effect of the common ion. The question whether the higher velocities in the presence of alkali are due to an ionic-strength effect or to some incursion of a bimolecular mechanism is thus not resolved and further investigations of the effects of added salts are necessary. Lucas and Hammett (*loc. cit.*) only detected acceleration by sodium hydroxide in solvents of high dioxan content. If the presence of excess of alkali gives rise to some bimolecular reaction the values obtained in No. 1 (where the ratio (KOH]/[Bu^{t}NO$_3$] = ~4) may not be strictly comparable with those of Nos. 2 and 4 (in which the ratio is ~2), with consequent repercussions on the derived values of the Arrhenius energies of activation.

Although the trend is somewhat irregular there is a general indication that the proportion of olefin formed increases with rise in reaction temperature, in agreement with the larger energy of activation of the $E1$ compared with that of the S_N1 reaction, and it is clear that the proportion of olefin formed is also greater in alkaline hydrolysis than in neutral solvolysis.

TABLE 7. *Alkaline hydrolysis and neutral solvolysis of* Bu^{t}NO$_3$ *in* 60% EtOH.

Initial concns. (mole l.$^{-1}$)			10^5k_1 (sec.$^{-1}$)			E (kcal./mole)		Reaction proportions, %	
[OH$^-$]	[Bu^{t}NO$_3$]	Temp.	S_N1	$E1$	Total	S_N1	$E1$	S_N1	$E1$
0·106	0·0289	20°	236	29·4	265	25·0	25·6	88·9	11·1
—	—	10	(43·7)	(6·3)	(50) *			(87·4)	(12·6)
0·101	0·0395	8·6$_5$	32·6	4·95	37·5			86·8	13·2
0·0866	0·0419	0	10·2	1·1	11·3			90·2	9·8
0	0·0272	30	589	51·9	641	21·2	23·0	91·9	8·1
0	—	20	(170)	(14·6)	(185)			(92·0)	(8·0)
0	0·0330	10	43·2	3·9	47·1			91·7	8·3
0	0·0372	0	12·5	0·80	13·3			94·0	6·0

* The values in parentheses have been calculated from the straight-line plots of $1/T$ against $-\log k$, for comparison with values at corresponding temperatures in the other series.

In the more highly ionising 60% alcohol there is a much closer general parallelism between the results for both alkaline hydrolytic and solvolytic decompositions, indicating that substitution and elimination reactions are proceeding essentially by the same mechanisms in both media. The results are summarised in Table 7.

It will be seen that the proportion of olefin formation in both alkaline and solvolytic reactions is less in 60% than in 90% alcohol (Table 6), but that again it is somewhat higher in the presence of hydroxyl ions.

It should be noted that the velocities of both the alkaline hydrolysis and the solvolysis of *tert.*-butyl nitrate are very much higher in the more highly ionising solvent, 60% alcohol.

Experimental

Solvent.—Absolute ethyl alcohol was dried and purified by refluxing it with sodium and ethyl phthalate (Smith, *J.*, 1927, 1288) and finally distilling it over solid 2 : 4-dinitrophenylhydrazine to remove the last traces of carbonyl derivatives. The resulting alcohol gave no appreciable reaction for aldehyde with Tollens's ammoniacal silver nitrate reagent. The solvent was prepared by mixing x volumes of this dry alcohol with $(100 - x)$ volumes of water to give "x vol.%" alcohol.

Preparation of Organic Nitrates.—Ethyl and *iso*propyl nitrates were prepared by adding ethyl iodide or *iso*propyl bromide, respectively, to dry, finely powdered AnalaR silver nitrate (slightly more than 1 molecular proportion) at 0°. The mixture was gently refluxed, with occasional addition of more powdered silver nitrate, to a total of 2 molecular proportions, until no alkyl halide remained and the liquid ceased to reflux at the b. p. of the alkyl halide. The product was distilled from the reaction mixture at ~50° under reduced pressure, condensed in a well cooled receiver, dried over anhydrous calcium nitrate in the presence of a little powdered calcium carbonate (to ensure freedom from acid), and carefully fractionated over fresh powdered silver nitrate. The main fraction (ethyl nitrate, b. p. 47°/180 mm.; *iso*propyl nitrate, b. p. 47°/105 mm.) was frozen in liquid air, then allowed partly to melt, and the liquid portion was removed by suction through a sintered-glass filter stick. The remaining crystalline material, after melting, was again dried over calcium nitrate and carefully refractionated from a little silver nitrate through a short column. The samples used were: ethyl nitrate, b. p. 49·8—50·0°/180 mm. (Found: C, 26·8; H, 5·9. Calc. for $C_2H_5O_3N$: C, 26·4; H, 5·5%); *iso*propyl nitrate, b. p. 49·5°/100 mm. (Found: C, 34·9; H, 6·8. Calc. for $C_3H_7O_3N$: C, 34·3; H, 6·7%).

For the prepation of *tert.*-butyl nitrate, refluxing must be avoided. *tert.*-Butyl chloride, mixed with an equal volume of pure dry ether, was shaken with an excess of dry powdered silver nitrate in the dark until the liquid was free from chlorine (~3 days). The ethereal solution was filtered from the silver salts, and the ether removed at room temperature under reduced pressure. The residue was distilled from a little powdered silver nitrate and calcium carbonate, the fraction of b. p. 23—25°/10 mm. being collected in a receiver cooled in an alcohol–solid carbon dioxide mixture. Purification was effected by the freezing technique previously described. The sample used had b. p. 21—23°/10 mm., m. p. *ca.* −36°, and gave consistent values ~100% purity by complete hydrolysis. It was stored, frozen solid, in small sealed brown ampoules in solid chest containing carbon dioxide (Lucas and Hammett, *loc. cit.*).

Methyl nitrate was available in accurately standard 0·06M-solutions in the purified 90% and 60% alcohol, which were stored below 0°. Owing to the very slow rate of solvolysis of this nitrate, no significant change occurs in these solutions over long periods at room temperatures. The zero point of each kinetic determination was always determined by actual titration. The infinity values after alkaline hydrolysis corresponded to a purity of ~100%.

Velocity Determinations.—In the case of the slowly reacting methyl, ethyl, and *iso*propyl nitrates, solutions of the nitrate and of potassium hydroxide of appropriate concentrations were mixed at room temperature (~20°) and the required volume of the reaction mixture was measured between calibration marks of a gravity-filled pipette ground into an all-glass apparatus, and suitably connected to a capillary delivery tube, by means of which the reaction vessels were filled. After the vessels had attained temperature equilibrium in the thermostat the concentration was checked by an initial zero reading. At suitable time intervals the vessels were chilled in ice, the lining vessels carefully removed, and the contents washed out with distilled water.

The sample was extracted with neutral ether, to remove unchanged organic nitrate, and the aqueous liquor, together with three aqueous washings of the ethereal extracts, was titrated with standard sulphuric acid (~0·03N) to methyl red, from a calibrated, microburette. The neutralised liquor, after appropriate concentration, was used for the gravimetric determination of nitrate as nitron nitrate. When nitrite was determined, the aqueous extract was made up to a suitable standard volume before titration and an aliquot portion used for the Griess–Ilosvay determination of nitrite, and the remainder was titrated and used for the nitrate determination.

The much greater speed of hydrolysis of *tert.*-butyl nitrate necessitated a different technique. Since the reaction is complete before appreciable alkali attack on glass occurs, the *tert.*-butyl nitrate was weighed directly from a weight-pipette into the appropriate volume of ~0·1N-potassium hydroxide solution in aqueous alcohol in a stoppered glass flask which had previously attained temperature equilibrium in the thermostat. After thorough mixing, a 2-c.c. sample was immediately taken within the first minute, for determination of the initial acidity (always present) of the organic nitrate, and this titre and time were taken as the zero values. In the alkaline hydrolysis in 90% alcohol separation of potassium nitrate occurs as the reaction proceeds and 2-c.c. samples were taken at appropriate time intervals with a pipette to the end of which was attached a sintered-glass filter stick. Time intervals were measured to the nearest second, on a stop-clock. In some alkaline hydrolyses, 0·12% of nitrite was found to be present. According to our suggested mechanisms, the elimination of nitrite (E_{CO} reaction) is impossible with this *tert.*-nitrate, and it was found that the amount present did not increase during the reaction and for long periods after its completion. Duplicate experiments in alkali, but on the same sample of *tert.*-butyl nitrate which had previously been allowed to age at room temperature for 2 and 9 days gave, respectively, 0·16 and 4·4% of nitrite, these amounts also remaining unchanged as the hydrolysis went to completion. It is thus evident that the small amount of nitrite formed is not a product of the hydrolytic decomposition but arises from slight decomposition of the initial sample of tertiary nitrate.

In the rapid neutral solvolysis, addition of calcium carbonate was considered unnecessary and the reaction was followed by acid–alkali titration, with only an occasional check by gravimetric determination of nitrate ion formed in experiments in 60% aqueous alcohol where the whole of the potassium nitrate formed remained in solution.

(1) *Nitrite.* The standard procedure was to treat 20 c.c. of the nitrite solution (~0·4—4·0 × 10^{-5}M) with 1 c.c. of each of the Griess–Ilosvay reagent solutions, warm the whole for 1·5 minutes at 70°, cool it to room temperature, allow it to stand for 2 minutes, and then determine the percentage transmission in a 1-cm. cell, using a OB1 blue light filter in a Hilger absorptiometer. The nitrite concentration was determined from a calibration curve based on the following data, obtained under identical experimental conditions, from standard solutions of AnalaR potassium nitrite.

$10^5[NO_2^-]$ (mole $l.^{-1}$)	7·55	3·77	2·83	1·89	0·94$_4$	0·37$_7$
Transmission, %	39·2	59·4	66·2	76·6	87·4	94·2

(2) *Nitrate.* A solution, ~0·025M in NO_3^-, was concentrated on a steam bath to 4·0 c.c. (after filtration, where necessary, to remove traces of precipitated indicator). To the hot solution 3 drops of glacial acetic acid were added, followed by 25 drops of a standard solution containing 10 g. of nitron in 100 c.c. of 5% acetic acid, stored in the dark. The tube was stoppered and the mixture allowed to cool in the dark for 20 minutes and then kept at 0° for 30 minutes. For concentrations <0·025M, the volume of solution and the quantity of reagent were decreased proportionately and a longer period was allowed for crystallisation of the nitron nitrate. The precipitated nitron nitrate was collected in a weighed, sintered-glass microcrucible, washed several times with small volumes of a saturated aqueous solution of nitron nitrate, dried at 112° for 30 minutes and weighed on a semi-micro-balance. With the factor NO_3^-/nitron nitrate = 0·1654, this technique gave the values NO_3^- = 61·2, 61·6, 60·6 (mean = 61·1) for AnalaR potassium nitrate (Calc. : NO_3^-, 61·4%), and was shown to be reliable when a 0·04995M-KNO_3 solution in 60% alcohol containing 0·03028M-ethyl nitrate was put through the usual ether-extraction technique (Found : NO_3^-, 0·04989M). A second sample containing 0·00509M-NO_3^- gave an equally satisfactory result (Found : NO_3^-, 0·00508M). Nitrite, when also present, was first destroyed with hydrazine sulphate or sulphamic acid. By this method a solution originally 0·0301M in potassium nitrate and 0·0189M in potassium nitrite gave NO_3^- = 0·0309M.

(3) *Olefin determination.* Three techniques were employed.

(i) Using sealed glass bulbs for the reaction. This was an earlier technique employed before the method (iii) (below) was developed, or in cases where alkali attack on glass was slight as in rapid reactions or neutral solvolysis. Sample bulbs (*B*) of the reaction mixture were removed from the thermostat after various times, then chilled, a small glass collar (*C*) was slipped over the neck of the bulb, and the whole dropped carefully into the lower section of the stoutly constructed glass apparatus shown in Fig. 2, which contained sufficient 2N-sulphuric acid to neutralise the alkali present in the reaction mixture, and 5 c.c. of carbon tetrachloride. After

the whole had been cooled in ice the point of the stout glass plunger *P* was inserted between the collar and the neck of the bulb and a sharp blow on the top of the plunger then *simultaneously* broke the bulb and closed the gas-tight glass stoppered joint *S* securely into its seat, thus completely sealing the lower portion of the vessel and preventing any possible escape of volatile olefin. The top portion was immediately sealed by means of the tightly fitting rubber stopper *A*.† The lower section was then well cooled in ice and a known (excess) volume of a 0·05N-solution of bromine in carbon tetrachloride saturated with hydrogen bromide was introduced through *T* into the top section. By slightly raising the stopper *S* this solution was sucked into the lower half, *S* being closed whilst a small volume of the solution still remained in the top half. A solution of potassium iodide was then introduced through *T* to ensure that no bromine escaped from this excess bromine solution. The olefin solution was allowed to react with the added bromine for 30 minutes, and, by using the same technique, the potassium iodide solution was then sucked in. The vessel was then opened, the whole contents were washed out, and the liberated iodine was titrated with 0·05N-sodium thiosulphate. The method was tested with weighed amounts of trimethylethylene (sealed in glass bulbs). Determinations gave 95, 93, 94, 96, 104% of olefin.

(ii) This technique was used for rapid hydrolytic reactions, such as those of *tert.*-butyl nitrate, in which the reaction is complete before any appreciable alkali attack on the glass vessel occurs. The actual reaction was carried out (to completion) in the lower section of an apparatus very similar to that depicted in Fig. 2, but without the plunger *P*. The olefin formed was then determined in the whole reaction mixture by a similar technique. The presence of acetone in concentrations far in excess of any likely to be produced by any $E_{co}2$ reaction, was shown not to introduce an error greater than that of the accuracy of the method. This technique was also tested with a standard alcoholic solution of *iso*butene, which was determined (*a*) by direct titration and (*b*) after submission to the reaction conditions in the thermostat for 70 hours. The following results show the amount of olefin in a 2-c.c. sample in terms of c.c. of ~0·01N-thiosulphate :

Method (*a*)	19·84	19·94	19·94	19·94
Method (*b*)	22·35	22·25 *	21·96	21·64 *
Found, %	113	112	110	109

Results marked * were obtained with olefin solution which had been mixed with an equal volume of 0·03M-nitric acid in alcohol whilst in the thermostat. The agreement with the other values shows that no appreciable loss of olefin by hydration occurs under the acid conditions produced in the solvolysis experiments.

(iii) An aspiration method was developed using a " Polythene " " test-tube ", constructed from " Polythene " rod of 1" diameter, and sealed with a two-holed rubber stopper through which passed a " Polythene " delivery tube, reaching to the bottom, and a glass exit tube (Fig. 3). A glass tube extension to the " Polythene " tube was secured by means of rubber. The reaction mixture was placed in the " Polythene " test-tube, the rubber stopper was sealed with wax, and the two glass tubes were drawn out and sealed at *A* and *B*. The vessel was immersed in the thermostat for the necessary period. To determine the olefin formed, *A* was connected to a supply of pure nitrogen and *B* was attached through an efficient trap, cooled to −12°, to a bubbler train containing a known volume of a standard solution of bromine in carbon tetrachloride and a guard-tube bubbler containing potassium iodide solution. The sealed glass tips *A* and *B* were then broken inside the connecting rubber tubing and a slow stream of nitrogen was passed through for 1 hour. The excess of bromine was determined with potassium iodide and standard thiosulphate solution in the usual manner. A " blank " correction for any alcohol vapour carried over into the bromine solution was carried out, with only solvent alcohol in the reaction vessel and the same rate of passage of nitrogen. The method was tested with a standard solution of pure propylene in alcohol against the olefin concentration determined by direct titration. In two experiments, the olefin in a 2-c.c. sample required the following volumes (c.c.) of 0·01N-bromine : Direct method, 8·53, 8·83. Aspiration method (iii), 9·38 (110%), 9·94 (113%).

Kinetic Results.—Details of typical kinetic experiments are recorded as illustrative of the general results. The data so given have not been corrected for solvent expansion.

† Initially a second glass-stoppered joint was employed here, but the resultant rigidity of the apparatus resulted in frequent fracture during breaking of the bulb and simultaneous closing of both glass-stoppered joints.

Methyl nitrate.

(a) Alkaline hydrolysis in 60% EtOH *at* 60·2° *in "Polythene" vessels.*

Initial $[MeNO_3] = 0·0301$; $[KOH] = 0·0854$M. Reaction followed by titration with 0·0378N-H_2SO_4 and by gravimetric determination of NO_3^- as nitron nitrate.

Time (mins.)	Vol. (c.c.) of H_2SO_4 for 4-c.c. sample	10^2x (mole l.$^{-1}$) OH^-	10^2x (mole l.$^{-1}$) NO_3^-	10^4k_2 (mole^{-1} l. sec.$^{-1}$) OH^-	10^4k_2 (mole^{-1} l. sec.$^{-1}$) NO_3^-
0	9·047	—	—	—	—
36	8·953	0·089	0·125	(1·66)	2·41
101	8·722	0·307	0·332	2·14	2·29
150	8·592	0·430	0·467	2·06	2·28
305	8·167	0·831	0·821	2·18	2·15
497	7·766	1·209	1·16	2·19	2·07
1320	6·848	2·076	1·96	2·04	1·81
∞ (11 days)		3·07 (102%)		(Mean) 2·14	2·17

Nitrite was only just detectable, ~0·1% of total reaction.

(b) Solvolysis in 90% EtOH *at* 96·2° *(mean temp. of boiling-water bath in "Monax" glass bulbs).*

Initial $[MeNO_3] = 0·0300$M.

Time (hours)	10^2x (mole l.$^{-1}$) H_3O^+	10^2x (mole l.$^{-1}$) NO_3^-	10^6k_1 (sec.$^{-1}$) H_3O^+	10^6k_1 (sec.$^{-1}$) NO_3^-
13·18	0·338	0·367	2·53	2·77
21·25	—	0·562	—	2·70
27·00	0·695	0·710	2·73	2·78
42·67	0·921	0·940	2·38	2·45
50·50	1·15	1·04	2·66	2·34
			Mean 2·58	2·61

The weighed amount of pure AnalaR calcium carbonate was different in each bulb, being graded to the amount of acid liberated at the time the sample was to be removed from the thermostat. Illustrative data for the sample taken at 13·18 hours in the above experiment are as follows:

(1) For determination of $[H_3O^+]$ produced. Wt. of $CaCO_3 = 0·00083$ g. ≡ 1·66 c.c. of 0·010N-HCl. 2-C.c. reaction sample required 0·984 c.c. Therefore, acid produced on hydrolysis ≡ 0·676 c.c. of 0·01N-HCl, whence $x = 0·676 \times 0·01 \times 500/1000 = 0·00338$ mole/l.

(2) For determination of $[NO_3^-]$ formed. Wt. of $CaCO_3 = 0·00079$ g. Acidified with acetic acid. Wt. of nitron nitrate from 2-c.c. sample = 0·00275 g., whence $[NO_3^-] = 0·00275 \times 0·1654 \times 500/62 = 0·00367$ mole/l.

Ethyl nitrate.

(a) Alkaline hydrolysis in 60% EtOH *at* 60·2° *in "Fluon" vessels.*

Initial $[EtNO_3] = 0·0306$; $[KOH] = 0·0904$M. Reaction followed by titration with 0·0287N-H_2SO_4 and by gravimetric determination of NO_3^- as nitron nitrate.

Time (hours)	Vol. (c.c.) of H_2SO_4 for 4-c.c. sample	10^2x (mole l.$^{-1}$) OH^-	10^2x (mole l.$^{-1}$) NO_3^-	10^5k_2 (mole^{-1} l. sec.$^{-1}$) OH^-	10^5k_2 (mole^{-1} l. sec.$^{-1}$) NO_3^-
0	12·589	—	—	—	—
8·13	12·313	0·198	0·197	2·58	2·58
17·00	12·114	0·341	0·374	2·17	2·37
32·00	11·740	0·609	0·640	2·21	2·34
49·50	11·321	0·910	0·935	2·32	2·42
70·00	11·006	1·14	1·20	2·20	2·36
93·50	10·680	1·37	1·38	2·13	2·16
			(NO_2^- = 0·013)		
118·2	10·339	1·61	1·65	2·16	2·25
				Mean 2·25	2·35

(b) Solvolysis in 90% EtOH *at* 59·3° *in "Monax" glass bulbs.*

Initial $[EtNO_3] = 0·0323$M.

Time (hours)	10^2x (mole l.$^{-1}$) H_3O^+	10^2x (mole l.$^{-1}$) NO_3^-	10^5k_1 (sec.$^{-1}$) H_3O^+	10^5k_1 (sec.$^{-1}$) NO_3^-
278·9	0·0947	—	2·98	—
998·5	0·277	0·353	2·50	3·22
1861	0·536	0·620	2·71	3·18
3087	1·16	1·02	(4·01)	3·41
			Mean 2·73	3·27

Olefin determination [method (iii) (p. 1204)]. Alkaline hydrolysis of ethyl nitrate in 90% EtOH at 59·3°. Initial $[EtNO_3] = 0·0343$; $[KOH] = 0·0975$M. 10 C.c. of reaction mixture in thermostat at 59·3° for 71·58 hours: 15 c.c. of standard bromine solution in carbon tetrachloride required (1) initially 17·40, (2) after aspiration of ethylene 16·68, and (3) blank (solvent only) 17·52 c.c., whence ethylene formed ≡ 0·72 c.c. of 0·0090N-sodium thiosulphate. Analysis of the reaction mixture for nitrate and nitrite gave $[NO_3^-] = 0·0165$, $[NO_2^-] = 0·0009$, $[C_2H_4] = 0·00033$ mole/l., whence $NO_2^- = 5$, $C_2H_4 = 2\%$ of total reaction.

iso*Propyl nitrate.*

(*a*) *Alkaline hydrolysis in* 90% *alcohol at* 60° *in "Polythene" vessels.*

Initial $[Pr^iNO_3] = 0·0343$; $[KOH] = 0·0983$M. Titration with 0·0247N-H_2SO_4.

Time (hours)	Vol. (c.c.) of H_2SO_4 for 2-c.c. sample	10^2x (mole l.$^{-1}$)				10^6k_2 (mole^{-1} l. sec.$^{-1}$)			
						Total			
		OH^-	NO_3^-	NO_2^-	$NO_3^- + NO_2^-$	OH^-	$NO_3^- + NO_2^-$	$E_{CO}2$ NO_2^-	$S_N2 + E2$
0	19·873	—	—	—	—	—	—	—	—
65	18·528	0·666	0·360	(0·056)	0·416	(9·72)	6·27	0·84	5·43
137	18·023	0·915	0·662	(0·102)	0·764	6·73	5·93	0·89	5·14
209·5	17·418	1·22	0·983	(0·152)	1·135	6·32	6·38	0·86	5·52
306·5	16·279	1·78	1·26	(0·194)	1·450	7·52	6·16	0·82	5·34
83 days	13·59	3·11	2·48	(0·387) *	2·732	—	—	—	—
∞	12·77	3·52	2·75	0·425	3·172	—	—	—	—
					Mean	(6·84)	6·18 ±0·14	0·85 ±0·02	5·36 ±0·12

* The values of $10^2[NO_2^-]$ in parentheses have been calculated from the experimental values of $10^2[NO_3^-]$ by using the ratio NO_2^-/NO_3^- determined at infinity, which is regarded as the most reliable. Actual determination of the value at 83 days gave $10^2[NO_2^-] = 0·350$.

Olefin determinations for above reaction. The aspiration method (iii) was used.

(1) Initial $[Pr^iNO_3] = 0·0433$; $[KOH] = 0·0983$M. After 72·97 hours at 60°, 10 c.c. of reaction mixture absorbed bromine ≡ 2·55 c.c. of 0·00903N-$Na_2S_2O_3$; blank (solvent only) required 0·76 c.c.; whence olefin ≡ 1·79 c.c. ≡ $0·81 \times 10^{-3}$ mole/l.

(2) Initial $[Pr^iNO_3] = 0·0422$; $[KOH] = 0·102$M. After 71·42 hours at 60°, 10 c.c. of reaction mixture absorbed bromine ≡ 2·37 c.c. of 0·000903N-$Na_2S_2O_3$; blank (solvent only) required 0·48 c.c.; whence olefin ≡ 1·89 c.c. ≡ $0·85 \times 10^{-3}$ (mole/l.). Analysis of the same reaction samples for NO_3^- thus gave

Time (hours)	10^2x (mole/l.) NO_3^-	C_3H_6	$100\,E2/(S_N2 + E2)$
(1) 72·97	0·495	0·081	16·3
(2) 71·42	0·490	0·085	17·4 } Mean = 16·8%

which, combined with above values for $10^6k(E_{CO}2)$ and $10^6k(S_N2) + E2$ gives

$10^6k(E2) = 0·90 = 14·5\%$ of total reaction
$10^6k(S_N2) = 4·46 = 71·8\%$,, ,,
$10^6k(E_{CO}2) = 0·85 = 13·7\%$,, ,,

(*b*) *Alkaline hydrolysis in* 60% *aqueous alcohol at* 60·2° *in "Fluon" vessels.*

Initial $[Pr^iNO_3] = 0·0347$; $[KOH] = 0·0916$M.

[This experiment clearly illustrates the greatly improved agreement between determinations of OH^- and NO_3^- in "Fluon" vessels. Nitrite formation ($E_{CO}2$) is only ~1% and no olefin formation could be detected after 92 hours (~50% reaction).]

Time (hours)	10^2x (mole l.$^{-1}$)			10^5k_2 (mole^{-1} l. sec.$^{-1}$)		10^6k_1 (sec.$^{-1}$)
	OH^-	NO_3^-	NO_2^-	OH^-	NO_3^-	NO_3^-
40·7	1·05	1·07	—	2·86	2·93	2·46
50·2	1·22	1·26	—	2·82	2·95	2·40
65·0	1·46	1·50	—	2·80	2·91	2·33
88·7	1·82	1·87	0·018	2·87	3·00	2·33
117·3	2·18	2·19	—	2·99	3·01	2·34

tert.-*Butyl nitrate.*

(*a*) *Alkaline hydrolysis in* 60% EtOH *at* 0°.

Initial [Bu^tNO_3] = 0·0419; [KOH] = 0·0866M.

Time (mins.)	10^2x (mole l.$^{-1}$) OH^- (found)	OH^- (corr.) *	NO_3^-	10^4k_1 (sec.$^{-1}$)
0	1·16	0	—	—
8·75	1·36	0·20	—	1·26
18·62	1·53	0·37	—	1·15
25·97	1·59	0·43	—	0·96
34·27	1·78	0·62	—	1·10
58·17	2·18	1·02	—	1·17
∞ (20 hrs.)	4·56	—	4·36	—
			Mean	1·13

(*b*) *Solvolysis in* 60% EtOH *at* 10°.

Initial [Bu^tNO_3] = 0·0330M.

Time (mins.)	10^2x (mole l.$^{-1}$) H_3O^+ (found)	H_3O^+ (corr.)*	NO_3^-	10^4k_1 (sec.$^{-1}$)
0	1·041	0	1·01	—
4·0	1·22	0·179	—	(3·45)
9·63	1·58	0·539	—	4·71
15·01	1·80	0·759	—	4·55
19·98	2·02	0·979	—	4·73
24·57	2·28	1·14	—	4·78
29·51	2·33	1·29	2·23	4·80
			Mean	4·71

* 10^2x (corr.) ≡ true amount of reaction subsequent to zero reading.

(*c*) *Hydrolysis in* 90% EtOH *at* 20° *in solution initially alkaline and becoming acid.*

Initial [Bu^tNO_3] = 0·0486; [KOH] = 0·0109M.

Time (mins.)	10^2x (mole l.$^{-1}$) H_3O^+ (found)	H_3O^+ (corr.)	NO_3^-	10^5k_1 (sec.$^{-1}$)
0	0·707	0	—	—
11·85	0·885	0·178	—	(6·15)
35·75	1·060	0·353	—	4·13
56·75	1·23	0·527	—	3·98
93·53	1·61	0·904	—	4·38
119·5	1·77	1·07	—	4·15
246·9	2·68	1·96	—	4·31
∞ (43 hrs.)	5·08	—	4·85	—
			Mean	4·19

Olefin determinations in above reactions. Owing to the higher b. p. of *iso*butene the aspiration method could not be used. Method (ii) (p. 1204) was used and it was found essential to cool the bottom half of the vessel to *ca.* −15° and then to admit sufficient acid to neutralise the alkali present immediately before admission of the bromine solution. Since all the samples of *tert.*-butyl nitrate used showed considerable acidity, and rapid hydrolysis occurs immediately the nitrate is added to the alkali solution, the percentage of olefin formed was calculated on the unchanged *tert.*-butyl nitrate present at zero time as determined by the initial acidity correction. In view of such necessary corrections the olefin values for this nitrate are rather less certain, but the general orders of magnitude are considered to be essentially correct.

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218. *Hydrolytic Decomposition of Esters of Nitric Acid. Part II.* The Effects of Structural and Solvent Changes on the Substitution and Elimination Reactions which occur in the Hydrolysis of Primary, Secondary, and Tertiary Alkyl Nitrates.*

By John W. Baker and (Mrs.) D. M. Easty.

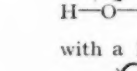
The data recorded in Part I (preceding paper) are used to effect a detailed analysis of the effects of (*a*) structure and (*b*) environmental factors on the rates of each of the three reactions S_N, E, and E_{CO} which occur side-by-side in the hydrolytic decomposition of methyl, ethyl, *iso*propyl, and *tert.*-butyl nitrates, and conclusions regarding mechanism are thus derived.

In the presence of hydroxyl ions in 90% alcohol the velocity sequence $Me > Et > Pr^i \ll Bu^t$ for nucleophilic substitution indicates a bimolecular mechanism for the primary and secondary nitrates and a unimolecular mechanism for the tertiary compound, which are confirmed by the effects of changes in solvent composition on the velocities. In neutral solvolysis the relative rates $Me > Et < Pr^i \ll Bu^t$ show superimposition of some unimolecular mechanism upon a predominantly bimolecular mechanism in the case of the *iso*propyl compound when either the ionising power of the solvent is increased or the nucleophilic power of the attacking reagent is reduced.

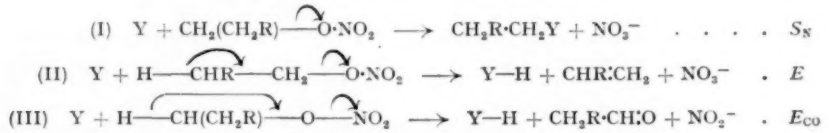
Olefin elimination confirms such mechanistic conclusions and is controlled by the electromeric effects of α- and β-substituents. The proportion of olefin is less with the nitrates than with the corresponding bromides.

The mechanism for carbonyl elimination is almost certainly bimolecular:

in which the β-atom of the system, from which the proton is removed, is the α-carbon atom of the nitrate. The *proportion* of carbonyl elimination, $Me \ll Et < Pr^i$, is also controlled by the electromeric effects of alkyl substituents, but the *rates* are in the order $Me \ll Et > Pr^i$ since, with the *iso*propyl compound in the carbonyl elimination the retarding inductive ($+I$) effect of *two* methyl groups acts directly on the β-atom, whereas in olefin elimination only a second-order $+I$ effect of *one* methyl substituent on the α-atom is relayed to the β-position.

The data previously obtained (Baker and Hemming, *J.*, 1942, 191; Baker and Hopkins, *J.*, 1949, 1087) for the values of k_2 in the (reversible) reaction make possible a preliminary comparison with a 1 : 2 elimination system , which is complementary to that  studied in these investigations.

The results recorded in Part I (preceding paper) clearly confirm the correctness of the view there enunciated that the hydrolytic decomposition of organic nitrates may involve the simultaneous occurrence of the reactions (I), (II), and (III):



All three reactions may occur by uni- or bi-molecular mechanisms depending on the degree of co-operation of the nucleophilic reagent Y in the rate-determining stage of the reaction. Kinetic analyses of such reactions for methyl, ethyl, *iso*propyl, and *tert.*-butyl nitrates,

* Part I, preceding paper.

have made possible a limited general survey of the effects of (1) structural changes in the alkyl group, and (2) environmental factors, on the relative importance and mechanisms of each of these separate reactions. All k values have been corrected for solvent expansion from room temperature (~20°) to the reaction temperature and are in the usual mole^{-1} l. sec.$^{-1}$ units.

(I) *The Substitution Reaction* S_N.—Of the various methods which have been devised to diagnose the mechanism of a substitution reaction (cf. Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979, for summary) only three can be applied on the basis of the data at present available for the hydrolysis of organic nitrates. These are the effect on reaction rate of (*a*) structural changes in the nitrate, (*b*) changes in the solvent, and (*c*) changes in the nucleophilic power of the attacking reagent.

(*a*) If the substitution reaction (I) proceeds by a bimolecular mechanism, the most probable effect of increasing the inductive electron-release of the group R in $R \rightarrow CH_2 \cdot O \cdot NO_2$ will be to decrease the rate, because the larger induced negative charge on the α-carbon atom will hinder the approach of the attacking nucleophilic reagent (the hydroxyl ion in alkaline hydrolysis). In the least ionising solvent, 90% alcohol, this is found to be the case for methyl, ethyl, and *iso*propyl nitrates, all of which follow the second-order rate law in the presence of hydroxyl ions. The relative rates in this solvent at 60° are :

	Me	Et	Pr^i
Relative rates	9·1 *	1	0·1
Arrhenius E (kcal./mole)	18·8	23·6	27·9

* In 75% alcohol : the value (not obtainable, see Part I) in 90% alcohol would be even higher (cf. Table 2).

The velocity order Me>Et>Pr^i is confirmed by the corresponding values of E, the Arrhenius energy of activation.

Introduction of a third α-methyl substituent, to give *tert.*-butyl nitrate, causes a marked change, since this nitrate undergoes very rapid hydrolysis, following a first-order rate law. Thus the half-life period for hydrolysis with ~0·09M-potassium hydroxide in 90% alcohol at 30° is 48 *minutes*, compared with a value of ~1876 *hours* for ethyl nitrate under the same conditions. It is evident that, with *tert.*-butyl nitrate, we have passed into the range of predominant, if not exclusive, unimolecular mechanism at least for the substitution reaction. This is confirmed by the observation that, in presence of only one-fifth of a molecular proportion of potassium hydroxide the first-order velocity coefficient remains constant throughout the whole reaction in which the medium, originally alkaline, becomes neutral and finally acid. It will be remembered that similar behaviour in the hydrolysis of *tert.*-butyl halides (Hughes, *J.*, 1935, 255) was the earliest evidence for the occurrence

TABLE 1. *Values of the first-order velocity coefficients* $10^5k(S_N1)$ (sec.$^{-1}$) *for* (a) *alkaline hydrolysis and* (b) *neutral solvolysis of* tert.*-butyl nitrate in aqueous alcohol.*

Solvent, aq. EtOH (vol. %)	Temp.	10^5k_1 (*a*)	10^5k_1 (*b*)	E (kcal./mole) (*a*)	E (kcal./mole) (*b*)
90	30°	18·5	13·9		
,,	20	4·93	3·1	22·3	22·6
,,	0	0·32	0·22		
60	30	(849)	589		
,,	20	236	(170)		
,,	10	(43·7)	43·2	25·0	21·2
,,	8·65	32·6	(38·9)		
,,	0	10·2	12·5		

The values in parentheses are calculated from the best straight-line plot of log k_1 against $1/T$.

of a unimolecular mechanism in substitution reactions. The essential independence of hydroxyl-ion concentration is also clearly demonstrated by a comparison, in Table 1, of the values of $10^5k_1(S_N1)$ for the *substitution* reaction in alkaline media with those for neutral solvolysis in the same solvents.

Although there may be some error in the various calculated values of 10^5k_1 (since the E values were determined from observations at only three temperatures and are derived

from an experimental analysis of the various simultaneous reactions), there can be no doubt that the presence of hydroxyl ions causes no *significant* increase in the velocity of the reaction which, in both media, is proceeding predominantly by a unimolecular mechanism

$$\left.\begin{array}{l} \mathrm{Bu^t{\cdot}O{\cdot}NO_2} \overset{\text{slow}}{\rightleftharpoons} {}^{+}\mathrm{Bu^t} + \mathrm{NO_3^-} \\ {}^{+}\mathrm{Bu^t} + \mathrm{ROH} \overset{\text{fast}}{\longrightarrow} \mathrm{Bu^tOR} + \mathrm{H^+}\ (\mathrm{R} = \mathrm{H\ or\ Et}) \end{array}\right\} \quad \ldots\ldots\ S_N1$$

The more highly ionising solvent 60% alcohol would be expected to shift the position of change-over from a bimolecular to a unimolecular mechanism more in the direction of smaller electron-release by the alkyl group, and there are clear indications that, in this solvent, there is considerable incursion of the unimolecular mechanism with *iso*propyl nitrate. The values of the second-order velocity coefficients (10^5k_2) at 60° for alkaline hydrolysis in 60% alcohol are Me 22·1, Et 2·35, Pr^i 2·98, *i.e.*, Me>Et<Pr^i.

In the neutral solvolysis the much weaker nucleophilic power of water or alcohol molecules would tend to favour the unimolecular mechanisms. Only very limited data are at present available but they indicate that in both 90% and 60% alcohol there is a velocity minimum at the ethyl compound, the values of 10^5k_1 at 60° being

	Me	Et	Pr^i	Bu^t
In 90% alcohol	$0{\cdot}007_3$	0·003	0·007	(367)
In 60% alcohol	0·0196	0·011	0·048	(14 450)

The order Me>Et<Pr^i≪Bu^t strongly suggests incursion of the unimolecular mechanism with the *iso*propyl compound, and exclusive unimolecular mechanism for the *tert.*-butyl nitrate. The values for the second-order velocity coefficients calculated on the basis of solvent–concentration and recorded in Part I (pp. 1199, 1200) point to the same conclusion. For methyl and ethyl nitrates the velocity for attack by the strongly nucleophilic hydroxyl ion is greater than that for attack by the neutral solvent molecules by a factor of 10^4 to 10^5, whilst this factor for *iso*propyl nitrate is only $\sim 10^3$. This point may be further illustrated by the application to our data, of the method used by Bateman, Cooper, Hughes, and Ingold (*J.*, 1940, 931) in the corresponding halide series illustrating the effect of adding a strongly basic reagent (KOH) to the solvent. If the concentration of alkali in the alkaline hydrolysis is regarded as buffered to 1N then the values of the second-order velocity coefficients become essentially first-order velocity coefficients and are thus directly comparable with the first-order constants in the solvolysis reaction, their sum giving a measure of the *total* reaction. In 60% alcohol at 60° the values are

		Me	Et	Pr^i	Bu^t
Solvolysis	10^5k_1	0·0196	0·011	0·048	(14 450)
KOH hydrolysis, buffered to 1N	10^5k_1	22·1	2·35	2·98	—
Total		22·1	2·36	3·03	(14 450)

Thus the reactions of methyl and ethyl nitrates are exclusively second-order, that of *iso*propyl nitrate is predominantly so, with a small incursion of a first-order reaction, whereas with the *tert.*-butyl compound the reaction is exclusively first-order. Thus the general picture in the series of alkyl nitrates is very similar to that for the alkyl halides, the position of change-over from bimolecular to unimolecular mechanism in aqueous-alcoholic solvents being located in the region of the *iso*propyl compound. Attention was called in Part I (p. 1195) to the much slower rate of hydrolysis of the alkyl nitrates than of alkyl bromides but such discrepancy is limited to the bimolecular mechanism: the rate of unimolecular hydrolysis of *tert.*-butyl nitrate is comparable in magnitude with that of *tert.*-butyl bromide. Thus the value 10^5k_1 (at 25°) = 37·2 for the bromide in 80% alcohol (Hughes and McNulty, *J.*, 1937, 1285) may be compared with those in 90% and 60% alcohol in Table 1. Examination of molecular models suggests that the reason for this much slower bimolecular hydrolysis of the nitrate is probably not steric in character since a large area of the α-carbon atom would seem to be exposed to nucleophilic attack. Pending further investigation, it seems more probable that it is due to repulsive forces between

the nucleophilic reagent and the negative charge field on the oxygen ends of the dipole in the nitrate group. A similar disparity was observed (Baker and Nathan, *J.*, 1936, 238) between the rate of quaternary salt formation of benzyl bromide and benzyl nitrate with pyridine in dry acetone at 40°, the values of 10^4k_2 being, respectively, 4·82 and 0·023 mole^{-1} l. sec.$^{-1}$. Our data for E for these reactions are not considered sufficiently extensive or accurate to warrant an attempt to analyse the effects of substitution on the A and E factors in the Arrhenius equation. The E values are of the same order as those for the alkyl halides.

(*b*) Evidence derived from the second diagnostic method, *viz.*, the effect of solvent changes, confirms the above conclusions regarding mechanism. Since the bimolecular mechanism with hydroxyl ions $\overline{HO} + RO{\cdot}NO_2 \longrightarrow \overset{\delta-}{HO}\cdots R\cdots\overset{\delta-}{O}{\cdot}NO_2 \longrightarrow HOR + \overline{NO_3}$ involves only a dispersal of the charge in the transition state, increase in the water content of the solvent should, on the Hughes–Ingold solvent theory (*J.*, 1935, 244), cause a small decrease in the velocity. This is found to be the case for methyl and ethyl nitrates (Table 2). In contrast, the velocity of hydrolysis of *iso*propyl nitrate is greater,

TABLE 2. *Effect of change of medium on the velocity coefficients* $10^5k_2(S_N2)$ *or* $10^5k_1(S_N1)$ *for alkaline hydrolysis of alkyl nitrates.*

Nitrate		Vol. % of water in the aqueous alcohol		
		10	25	40
$MeNO_3$	10^5k_2 at 60°	—	40·2	22·1
,,	,, at 44·8°	—	10·1	5·2
$EtNO_3$	10^5k_2 at 60°	4·1	—	2·35
,,	,, at 44·8°	0·98 *	—	0·47 *
Pr^iNO_3	10^5k_2 at 60°	0·46	—	2·98
Bu^tNO_3	10^5k_1 at 20°	4·93	—	236
,,	,, at 0°	0·32	—	10·2

* Total reaction ($S_N2 + E2 + E_{CO}2$).

and that of *tert.*-butyl nitrate very much greater, in the more highly ionising solvent. This is in harmony with the requirements of a unimolecular mechanism in which the transition state $\overset{\delta+}{R}\cdots\overset{\delta-}{O}{\cdot}NO_2$ involves an increase in the magnitude of the charge, the hydrolxyl ion not being involved in the rate-determining stage of the reaction.

(*c*) In neutral solvolysis, the same large velocity increase in the more highly ionising solvent is observed (Table 3) in the case of the tertiary nitrate (in agreement with the

TABLE 3. *Effect of change of medium on the velocity coefficients* $10^5k_1(S_N)$ *for neutral solvolysis of alkyl nitrates.*

	Vol. % of water in the aqueous alcohol	
	10	40
$MeNO_3$ at 60°	0·0073	0·0196
,, ,, ~97°	0·28	0·87
$EtNO_3$,, 60°	0·003	0·011
Pr^iNO_3 ,, 60°	0·007	0·05
Bu^tNO_3 ,, 30°	13·9	589
,, ,, 0°	0·22	12·5

requirements of the unimolecular mechanism) but the velocity of neutral solvolysis of methyl and ethyl nitrates, unlike those of the alkaline hydrolysis, is also higher in 60% than in 90% alcohol. This is expected since the bimolecular mechanism

$$HOR + R{\cdot}O{\cdot}NO_2 \longrightarrow \overset{\delta+}{HOR}\cdots R\cdots\overset{\delta-}{O}{\cdot}NO_2 \longrightarrow \underset{+}{\overset{H}{R}}OR + NO_3^- \ (\longrightarrow ROR + HNO_3)$$

involves an increase in the magnitude of the charge in the transition state, although the magnitude of the observed velocity increase is smaller than might have been expected.

*iso*Propyl nitrate also undergoes solvolysis more rapidly in the more aqueous solvent but the order of magnitude of the increase resembles those for methyl and ethyl nitrates

more closely than the large increases observed with the tertiary nitrate, for which all evidence supports a unimolecular mechanism.

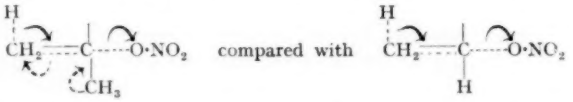
(II) *Olefin Elimination* E.—With ethyl and *iso*propyl nitrates significant olefin elimination only occurs in the alkaline hydrolysis and has not been detected in the neutral solvolysis of these compounds. This is in accord with a bimolecular elimination reaction for these two esters since a reagent of low nucleophilic power retains its capacity for attack at carbon long after it has ceased to be able to attack hydrogen. As would be expected from the unimolecular mechanism valid for *tert.*-butyl nitrate which, in both media, involves the formation of a *tert.*-butyl cation as the rate-determining stage, *iso*butene is formed in both alkaline hydrolysis and neutral solvolysis. In the halide series it is known that second-order eliminations of alkyl halides obey the Saytzeff rule and are controlled by the electromeric effect (Dhar, Hughes, Ingold, Mandour, Maw, and Woolf, *J.*, 1948, 2114). The major factor which determines that the hyperconjugative effect shall be predominantly in control, is the neutral character of the group subsequently eliminated as an anion. It would therefore be expected that the nitrates, in which the group $-O{\cdot}NO_2$, although containing a dipole, is formally neutral, would follow the same rule. If this is so, introduction of an α- or a β-methyl substituent should increase the rate and proportion of olefin elimination and hence, for the series studied, these should increase in the order $Et < Pr^i < Bu^t$. The *tert.*-butyl nitrate, however, undergoes unimolecular elimination which is also governed

TABLE 4. *Rate constants and proportions of olefin formed in the hydrolysis of* $CH_2{\cdot}CR_2{\cdot}O{\cdot}NO_2$ *with* ~0·1M-KOH *in* 90% EtOH.

α-Substituents (R_2)	Temp.	$100E_2/(S_N2 + E2 + E_{CO}2)$	$10^5k(E2)$	$10^5k(E1)$
H, H	59·3°	2	0·08	—
,,	30	4	0·006	—
H, Me	59·3	14·5	0·09	—
,,	79·7	11·1	0·72	—
Me, Me	59·3	~50 *	—	246 *
,,	30	23	—	5·5

* Calc. from the plots of $1/T$ against log $k(S_N1)$ and $k(E1)$.

by the Saytzeff rule so that, in spite of the change of mechanism, the given order should be maintained. Data in Table 4 clearly establish that, as α-methyl substituents are successively introduced into the molecule, the proportion of olefin formed does increase. This is ascribed to the resulting increased stabilisation due to hyperconjugation with the forming double bond in the transition stage (cf. Dhar *et al.*, *loc. cit.*, p. 2107):



The only data yet available regarding the effect of change of solvent on the olefin elimination reaction are those for *tert.*-butyl nitrate. The rate-determining stage in this unimolecular mechanism is the same for both the substitution and elimination reactions and involves the transition state

$$Bu^tO{\cdot}NO_2 \longrightarrow \overset{\delta+}{Bu^t}\cdots\overset{\delta-}{O{\cdot}NO_2} \longrightarrow \overset{+}{Bu^t} + \overset{-}{O{\cdot}NO_2}$$

in which the magnitude of the charge is increased. In accordance with the theory of solvent effect enunciated by Cooper, Dhar, Hughes, Ingold, MacNulty, and Woolf (*J.*, 1948, 2045) the value of 10^5k_1 for the total reaction ($S_N1 + E1$) should greatly increase as the proportion of water in the aqueous-alcoholic solvent is increased. This is found to be the case for reaction in both alkaline and neutral media. The data are in Table 5.

In the alkaline media $E1/S_N1$ depends on the relative effects of the ionising medium on the transition states in the *fast* reaction, $HO^- + \overset{+}{Bu^t} \longrightarrow \overset{\delta-}{HO}\cdots\overset{\delta+}{Bu^t} \longrightarrow Bu^tOH$ for S_N1, and $\overset{\delta-}{HO}\cdots H\cdots CH_2{=}\overset{\delta+}{C}Me_2 \longrightarrow H{\cdot}OH + CH_2{:}CMe_2$ for $E1$, in *both* of which there is a reduction of charge so that no prediction regarding the effect of change

in medium on the *proportion* of olefin elimination is possible. Experimentally it is found (Table 6) that there is less olefin formation in the more highly ionising solvent. In neutral solvolysis, the transition states of both the fast reactions, *viz.*, $\overset{\delta+}{\text{ROH}}\text{—}\overset{\delta+}{\text{Bu}^t} \longrightarrow \text{Bu}^t\overset{+}{\text{O}}\text{RH}$ for S_N1 and $\overset{\delta+}{\text{ROH}}\text{---H---CH}_2\text{---}\overset{\delta+}{\text{C}}\text{Me}_2$ for $E1$, are formed with dispersal of a given charge, which, however, is more extensive in the elimination reaction. It would thus be expected that, in the more aqueous alcohol, there would be a small decrease in the proportion of olefin formed by neutral solvolysis. Data in Table 6 confirm this.

TABLE 5. *Solvent effects on the values of* $10^5k_1(S_N1 + E1)$ *for* Bu^tNO_3 *in aqueous* EtOH.

	Vol. % of H_2O in aq. EtOH	
	10	40
~0·09M-KOH at 20°	6·47	265
,, ,, 0°	0·38	11·3
Solvent only ,, 30°	16·3	641
,, ,, 0°	0·25	13·3

TABLE 6. *Solvent effects on the ratio* $100E1/(S_N1 + E1)$ *in the hydrolysis of* Bu^tNO_3.

	Vol. % of H_2O in the aq. EtOH	
	10	40
~0·09M-KOH at 20°	23·8	11·1
,, ,, 0°	15·6	9·8
Solvent only ,, 30°	14·6	8·1
,, ,, 0°	12·8	6·0

Thus, from the admittedly limited data available it would appear that olefin elimination from ethyl and *iso*propyl nitrates occurs by a bimolecular mechanism but that from *tert.*-butyl nitrate is mainly, if not exclusively, unimolecular. All such eliminations are controlled predominantly by the electromeric effect of α- and β-alkyl substituents which, by hyperconjugation with the forming double bonds, lower the energy of the transition state and so increase the proportion of the olefin formed in the series $Et < Pr^i < Bu^t$.

(III) *Carbonyl Elimination*, E_{CO}.—The reaction (III), which is specific to alkyl esters of oxyacids such as nitric, involves the removal, as a proton, of the hydrogen attached to the α-carbon atom of the nitrate which is, of course, a β-hydrogen atom in the generalised scheme of 1 : 2-elimination reactions $\text{H—}\overset{\beta}{\text{a}}\text{—}\overset{\alpha}{\text{b}}\text{—X} \longrightarrow \text{a=b} + \text{HX}$, the α-atom being oxygen :

$$\text{H—}\overset{\beta}{\text{C}}\text{—}\overset{\alpha}{\text{O}}\text{—NO}_2 \longrightarrow \text{H}^+ + >\text{C=O} + \text{NO}_2^-$$

The question whether inductive or electromeric effects control such elimination is interesting. Since, in neutral solvolysis, at the most only a minute trace of nitrite is formed and the reaction is structurally impossible with *tert.*-butyl nitrate, we need only consider a bimolecular mechanism. It is in this mechanism that predominant control by either the inductive or the electromeric effect is determined essentially by the nature of the group X, whether it is initially positively charged or neutral, respectively (Dhar *et al.*, *loc. cit.*). In the case of the carbonyl elimination reaction this group X is $-\overset{+}{\text{N}}\!\!\begin{matrix}\diagup\,\text{O}^-\\ \diagdown\!\!=\text{O}\end{matrix}$ which, although formally neutral, carries an integral positive charge on the atom which is directly attached to the α-atom of the system. It has been suggested that the reason why bimolecular eliminations from alkyl-substituted 'onium compounds are controlled predominantly by the inductive effect (Hofmann rule) is because the strong electron attraction ($-I$) of the positive charge of the 'onium group, relayed through the α-carbon atom, stimulates the maximum operation of the $+I$ effect of any β-alkyl substituent. In the organic nitrates such relay of the $-I$ effect of the nitro-group occurs through an intervening unsaturated atom, bivalent oxygen, and it would thus be expected that its effect on C_β would be largely damped out. Hence we might expect that bimolecular carbonyl elimination from organic

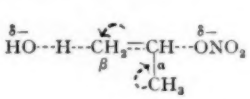
nitrates would be controlled predominantly by the electromeric effect, as is the case in the alkyl halides. This would require that, in the alkaline hydrolysis of $RO{\cdot}NO_2$, the proportion of $E_{CO}2$ reaction should run parallel to olefin formation and increase in the order, R = Me<Et<Pr^i. The data in Table 7 show that this is confirmed. With methyl nitrate, nitrite formation is barely detectable, with ethyl nitrate it is measurable, whilst with *iso*propyl nitrate it is comparable in importance to the olefin-elimination reaction.

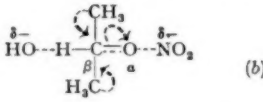
TABLE 7. *Proportion and values of* $10^5k(E_{CO}2)$ *for the carbonyl elimination reaction of* $RO{\cdot}NO_2$ *with* ~0·09M-KOH *in* 90% EtOH.

Nitrate	Temp.	$100E_{CO}2/(S_N2 + E2 + E_{CO}2)$	$10^5k(E_{CO}2)$
$MeO{\cdot}NO_2$ *	44·8°	~0·1	negligible
" *	60·2	~0·1	"
$EtO{\cdot}NO_2$	30	2·0	0·003
"	59·3	4·8	0·2
$Pr^iO{\cdot}NO_2$	59·3	13·7	0·09
"	79·7	8·5	0·55

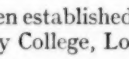
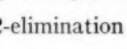
* In 75% EtOH.

In any comparison of the velocities, $10^5k(E_{CO}2)$, there is, however, another factor to be considered. In the carbonyl-elimination reaction the hydrogen removed as a proton is attached to C_α and the inductive (+*I*) effects of α-alkyl substituents, directly attached to the carbon from which proton elimination occurs, would exert a strong, first-order retarding effect on such ionisation. Such modifying influences of inductive effects on predominant control by the electromeric effect were noted by Dhar, Hughes, Ingold, *et al.* (*loc. cit.*) in elimination reactions of alkyl halides and sulphonium compounds. In our data they are revealed in the observation that, whilst the *proportion* of the $E_{CO}2$ reaction is much higher with *iso*propyl than with ethyl nitrate (as required by electromeric control), the value of $10^5k(E_{CO}2)$ is lower for the former compound (0·09 at 59·3°) than for the latter (0·2 at 59·3°). Thus the inductive effect (+*I*) of the two α-methyl substituents in *iso*-propyl nitrate greatly decreases the velocity of total reaction with hydroxyl ions ($S_N2 + E2 + E_{CO}2$), whilst the hyperconjugation effect with the forming double bond in the transition states of both olefin (*a*) and carbonyl (*b*) elimination reactions increases the

(*a*) 

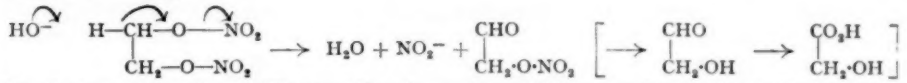
 (*b*)

proportion of these reactions in both cases by the relative lowering of the energy levels of the two transition states. With *iso*propyl nitrate, however, whereas in olefin elimination (*a*) the retarding inductive (+*I*) effect of *one* α-methyl substituent is relayed only in second-order magnitude to C_β (from which proton separation occurs) and so does not greatly affect the value of $k(E2)$, in the carbonyl reaction (*b*), the retarding inductive effects of *two* methyl substituents are operating *directly* on the β-atom of the system, *i.e.*, on the atom from which the proton separates, and hence greatly reduce the velocity of the $E_{CO}2$ reaction to a value lower than that for the corresponding reaction of ethyl nitrate, which carries only one such methyl substituent.

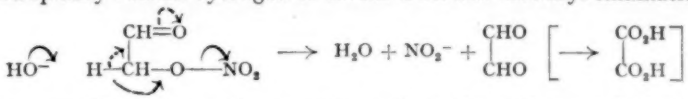
The overall picture of the mechanism of hydrolytic decomposition of simple alkyl nitrates is thus seen to fit in well to the general pattern of the theories of substitution and elimination reactions which have been established in such detail for the system  by the research school at University College, London, theories which are now shown to be capable of logical extension to 1 : 2-elimination from a system of the type  $\longrightarrow C{=}O + HX$ (X = NO_2).

The simultaneous occurrence of the three reactions, S_N2, $E2$, and $E_{CO}2$ also indicates the lines along which data in the early literature regarding the alkaline hydrolysis of poly-nitrates such as glycol dinitrate or glycerol trinitrate may be explained. The observed formation of nitrate, nitrite, glycollic acid, aldehyde resins, etc., might well follow from

oxidation of products initially formed by an $E_{CO}2$ type of reaction in accordance with schemes of the type :



The electron-attracting CHO group thus formed would then greatly facilitate the ionisation of the prototropically related hydrogen to favour a further carbonyl-elimination reaction,

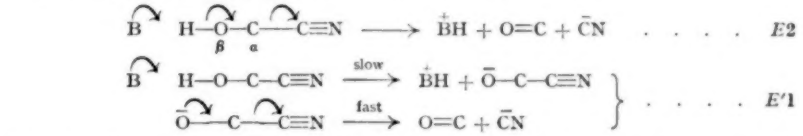


Such reactions would, of course, be superimposed on the ordinary substitution reaction giving nitrate ion and alcohol. Accurate kinetic examination of the decomposition of such polynitric esters must await the increase in our understanding of such reactions which should accrue from further studies of the effects of structural and environmental factors on the hydrolytic decomposition of simple mononitrates such as are already in hand.

In conclusion, there is an interesting comparison between the mechanism of E_{CO} elimination in the systems H—C(—O—X)—, discussed in this paper, and that of the complementary system H—O—C(—X)— $\longrightarrow$ O=C + HX, data for which are provided by the values of k_2 in the reversible reaction $R{\cdot}C_6H_4{\cdot}CHO + HCN \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R{\cdot}C_6H_4{\cdot}CH(OH){\cdot}CN$ (Baker and Hemming, *loc. cit.*; Baker and Hopkins, *loc. cit.*) which are as follows :

R =	*p*-	Bu^t	Pr^i	Et	Me	H	F	Cl	Br	I	NO_2
$10^{10}k_2$ at 20° (sec.$^{-1}$)		0·57	0·57	0·68	0·74	0·74	2·26	2·67	2·98	2·94	12·6
R =	*m*-						F	Cl	Br	I	NO_2
$10^{10}k_2$ at 20° (sec.$^{-1}$)							2·18	2·45	2·69	2·92	12·3

As was pointed out by Baker and Hopkins (*loc. cit.*) the dissociation of the cyanohydrin is retarded by electron release towards the carbon atom of the elimination system and facilitated by electron attraction from this carbon atom. Hence the rate-determining step can hardly be the anionisation of a cyanide ion from the cyanohydrin. Since the reaction is base-catalysed, two mechanisms can be considered :



The first is an ordinary bimolecular elimination mechanism. Since the group (CN) which ultimately separates with its bonding electrons is originally neutral it might be expected that, in this mechanism, as in the elimination of hydrogen halide from alkyl halides, substituents on the α-carbon atom would control the rate of elimination essentially by their electromeric effect, *i.e.*, their capacity to conjugate with the forming carbonyl double bond in the transition state. So far as the limited data available * show, there is no support for this view, since the effect of a nitro-group, in the common phenyl substituent, differs little whether it is in the *meta*- or the *para*-position. The values of k_2 for whole series of substituents clearly suggest that the controlling feature is the *inductive* effect of the substituent R. Bearing in mind Baker and Hopkins's conclusion (*loc. cit.*) that the superimposition of the $+M$ and the $-I$ effect of the halogen substituents satisfactorily accounts for an order of overall electron *attraction* F<Cl<Br~I, we have a continuous velocity increase as R changes from electron-releasing alkyl groups, through H, to groups with increasing $-I$ effects. Even with the alkyl substituents the small *retarding* effect decreases in the order R = (Bu^t ~Pr^i)>Et>Me which is essentially the order of

* *Velocity* data are not yet available for the various aliphatic ketone- and aldehyde-cyanohydrin equilibria studied by Lapworth and Manske (*J.*, 1930, 1978).

their decreasing $+I$ effects. It is for such reasons that, pending more diagnostic evidence regarding mechanism, the second mechanism $E'1$ is regarded as more probable. This is a unimolecular mechanism, but it differs from the usual $E1$ mechanism in that the rate-determining stage is the removal of a proton to give an ***anion***, in contrast to the usual anionisation of the group X leaving a carbonium ion. This difference in the mechanism of 1 : 2-elimination from the systems H—C—O—X and H—O—C—X is almost certainly related to the much greater ease of fission of a H–O than of a H–C or C–X bond. Electron attraction at the carbon atom, by increasing its positive character, will increase the strength of the cyanohydrin as an acid $H \rightarrow O \rightarrow \overset{\delta+}{C}(\downarrow R)—X$ and so increase k_2. It is intended to make a more extensive kinetic study of this system so that more effective comparisons may be possible.

THE UNIVERSITY, LEEDS. [*Received, October 12th*, 1951.]

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219. *Studies with Dithizone. Part IV.* The Dissociation Constant of Dithizone.*

By H. IRVING and C. F. BELL.

Measurements of the distribution coefficient of dithizone between a variety of organic solvents and aqueous buffers of known pH lead to the value $pK_{HDz} = 4{\cdot}5 \pm 0{\cdot}3$. A tapless apparatus has been devised for Golumbic and Weller's "interchange extraction" procedure, and a modification of this technique has been shown to be suitable for measuring very small partition coefficients.

IT has already been clearly established that the important analytical reagent diphenylthiocarbazone ("dithizone," HDz) behaves as a monobasic acid, at least up to pH 12 (Irving, Cooke, Woodger, and Williams, *J.*, 1949, 1847), but owing to its extremely low solubility in water (about 10^{-7}M) conventional methods cannot be used to measure the dissociation constant, $K_{HDz} = [H^+][Dz^-]/[HDz]$, and its value is still in doubt.

The value $pK_{HDz} = 5{\cdot}25$ was calculated (*loc. cit.*) from the known dissociation constants of methyl-red and bromothymol-blue in water and the values of the apparent dissociation constants of these indicators and of dithizone as determined spectrophotometrically in a homogeneous mixture of water, alcohol, and chloroform, on the assumption that change of solvent does not alter the relative order of magnitude of acid strengths—but this must be treated with some reserve (cf. Bayles, D.Phil. Thesis, Oxford, 1951).

An alternative method requires a knowledge of $p_o = [HDz]_w/[HDz]_o$, the partition coefficient of molecular dithizone between water and an immiscible organic phase, together with measurements at various pH's of p, the distribution ratio for this solute between aqueous buffers (in which it dissolves both as molecules, HDz, and as dithizonate ions, Dz^-) and an organic phase: it has been shown (*loc. cit.*) that K, p_o, and $pH_{\frac{1}{2}}$, the hydrogen-ion exponent for which p is unity, are related by the equation

$$pK = \log_{10} p_o + pH_{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The value of this method for determining the dissociation constants of sparingly soluble phenols has recently been demonstrated by Golumbic, Orchin, and Weller (*J. Amer. Chem. Soc.*, 1949, **71**, 2624), but its applicability to the case of dithizone depends upon the precision with which the component terms of equation (1) can be determined. So far as $pH_{\frac{1}{2}}$ is concerned there is very satisfactory agreement between the measurements of different observers (cf. Table 1), but values for the extremely small partition coefficient of undissociated dithizone are difficult to measure experimentally and the discrepancy between our value of $p_o = 6{\cdot}4 \times 10^{-4}$ for water/carbon tetrachloride and that of Sandell (*loc. cit.*), who recently reported $9{\cdot}1 \times 10^{-5}$, leads to the seriously discordant values for pK_{HDz} of 5·6 and 4·8, respectively.

* Part III, *J.*, 1952, 356.

TABLE 1.

$pH_{\frac{1}{2}}$	Temp.	Ref.	Comments
8·72	31°	*a*	One measurement at pH 10
8·90	~ 20	*b*	Nine measurements from pH 7·85 to 10
8·85	25	*c*	Determinations at pH 8 and 9
8·80	—	*d*	Seven determinations from pH 7 to 9
8·80	~ 20	*e*	Five determinations between pH 8·2 and 9·1 with buffers of ionic strength 0·14

[a] Clifford and Wichmann, *J. Assoc. Offic. Agric. Chem.*, 1936, **19**, 130. [b] Irving *et al.*, *loc. cit.* [c] Sandell, *J. Amer. Chem. Soc.*, 1950, **72**, 4660. [d] Buch and Koroleff, *Finska Kem. Medd.*, 1945, **54**, 98, quoted in *Chem. Abstracts*, 1950, **44**, 8750[d]. [e] Present authors.

In a reinvestigation of the dissociation constant of dithizone, we have modified the method of " interchange extraction " recently proposed by Golumbic and Weller (*Analyt. Chem.*, 1950, **22**, 1418) for the determination of very large (or very small) partition coefficients so as to avoid the complete separation of phases after each equilibration—an operation which presents considerable experimental difficulties. The basic procedure was as follows: 45 ml. of 0·1M-hydrochloric acid were equilibrated with 5 ml. of a concentrated solution of dithizone in the organic solvent under investigation by 1½ hours' shaking in a stoppered Pyrex test-tube. After the phases had separated, exactly 40 ml. of the aqueous phase were transferred to a second Pyrex test-tube and, after the addition of 5 ml. of 0·1M-hydrochloric acid and 5 ml. of pure organic solvent, equilibration was carried out as before. Simultaneously, equilibration was effected in the first tube after the addition of 40 ml. of 0·1M-hydrochloric acid. This completed the first interchange, at which stage each tube contained 5 ml. of organic phase and 45 ml. of aqueous phase; 40 ml. of each aqueous phase were then interchanged, and the equilibrations repeated. This completed the second interchange, and further stages of interchange were carried out in the same way. By interchanging a (large) aliquot portion rather than the whole of each aqueous phase at each stage, disturbance of the water–organic phase boundary was minimised and gross errors caused by the inadvertent transfer of droplets of the organic phase could be completely avoided. The necessary modification in Golumbic's quantitative treatment of the equilibria (*loc. cit.*) is shown in Table 2, which portrays the position at the end of each successive stage when V ml. of organic phase are equilibrated with nV ml. of aqueous phase, $V' < nV$ ml. being transferred at each interchange. For convenience, we write

TABLE 2.

Number of interchange, *m*.	Fraction of the total solute in: first tube	second tube
0	1	0
1	a/b	c/b
2	$(a^2 + c^2)/b^2$	$2ac/b^2$
3	$(a^3 + 3ac^2)/b^3$	$(3a^2c + c^3)/b^3$
. . . . .	. . . . .	. . . . .
m	$[a^m + m(m-1)a^{m-2}c^2/2! + m(m-1)(m-2)(m-3)a^{m-4}c^4/4! + \ldots]/b^m$	$[ma^{m-1}c + m(m-1)(m-2)a^{m-3}c^3/3! + \ldots]/b^m$

$R = V'/nV$, $a = 1 + (1 - R)np_o$, $b = 1 + np_o$, and $c = nRp_o$. It is clear from Table 2 that the *total* amount of solute in either tube at the end of each stage is obtained by taking the sum of alternate terms in the expansion of $(a + c)^m/b^m$; terms with even powers of c appearing in the expression for the first tube, and those with odd powers of c in that for the second tube. The fraction of each successive total amount present in the organic phase after equilibration is obtained by dividing the successive entries of Table 2 by the quantity $b = 1 + np_o$. In our experiments $R = 0{\cdot}89$, and the partition coefficient of dithizone was given by

$$\frac{\text{Dithizone concentration in the organic phase of the second tube after } m \text{ interchanges}}{\text{Dithizone concentration of the original organic phase in the first tube}} = [ma^{m-1}c + m(m-1)(m-2)a^{m-3}a^3/3! + \ldots]/b^m \cong 8mp_o$$

The magnitude of the quantity, p_o, to be measured is effectively magnified 8-fold at each exchange, and theoretically there is no reason why the process should not be continued until the concentrations of the organic extracts in the two tubes approach equality. In practice, since each stage of equilibration took 1½ hours, the process was terminated after comparatively few stages in order to minimise errors due to the gradual decomposition of the dithizone and the introduction of adventitious metallic impurities.

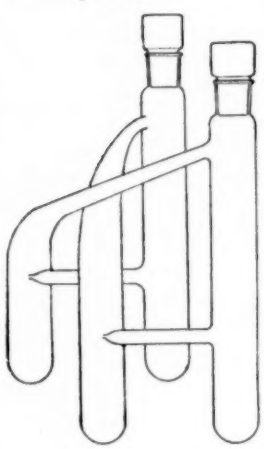
TABLE 3.

Solvent	$p_o \times 10^5$	$pH_{\frac{1}{2}}$	pK	Method
*cyclo*Hexane	43	7·44	4·1	*a*
*cyclo*Hexane	52	7·44	4·2	*b*
Carbon tetrachloride	9·1	8·85	4·8	*c*
Carbon tetrachloride	6·6	8·8	4·6	*b*
Benzene	1·3	9·09	4·2	*a*
Chloroform	1·3	10·58	5·7	*b*

[a] Approaching equilibrium from a supersaturated aqueous phase. [b] Interchange method. [c] Average value from Sandell (*loc. cit.*).

Since the solubility of dithizone in *cyclo*hexane (14 mg./l.) is much lower than in most other organic solvents (Irving and Tilley, to be published shortly), the partition coefficient should be proportionately increased and thus be more suitable for accurate measurements. Values of p_o were therefore obtained by the interchange method using the solvents *cyclo*hexane, carbon tetrachloride, and chloroform, and, as a further check, measurements of p_o were made with the solvents *cyclo*hexane and benzene, by the technique described by Sandell (*loc. cit.*) in which equilibrium is approached from a supersaturated aqueous phase. Of the results shown in Table 3, together with measured values of $pH_{\frac{1}{2}}$ and calculated values of pK, that for chloroform is clearly anomalous. The agreement between the values for *cyclo*hexane obtained by the two procedures confirms the reliability of the interchange technique, and the agreement between the value for carbon tetrachloride obtained by this method and the value reported by Sandell (*loc. cit.*) is not unsatisfactory, the discrepancy appearing almost entirely in the measured values of p_o. There can be little doubt that the value $p_o = 6{\cdot}4 \times 10^{-4}$ for carbon tetrachloride previously reported (Irving *et al.*, *loc. cit.*) was seriously in error owing to failure to reach equilibrium under the conditions employed when starting with a dilute organic solution of dithizone, and the value of pK reported in that paper should be discarded. However, it must be recognised that in these measurements we are in fact not measuring the dissociation constant of dithizone in water, but rather in a series of aqueous phases saturated with different organic solvents. Even so, the discrepancies between the values of pK derived from measurements with different water–solvent systems are disturbingly large, and at present it does not seem possible to give a more precise value for the dissociation constant of dithizone than $pK_{HDz} = 4{\cdot}5 \pm 0{\cdot}3$. It is, however, worth commenting on the fact that the biggest discrepancy occurs with chloroform, which is the most polar and the most water-soluble of the solvents studied.

Apparatus for interchange equilibration.



The apparatus shown (not to scale) in the figure was constructed to permit the processes of equilibration and phase-interchange incident to Golumbic and Weller's interchange extraction procedure to be carried out automatically and under conditions such that oxidation and the introduction of adventitious impurities could be avoided. It is an adaptation of the all-glass unit devised by Craig (*Analyt. Chem.*, 1950, **22**, 1346) for use in counter-current extraction work (cf. Irving, "Solvent Extraction and its Application to

Inorganic Analysis," *Quart. Reviews*, **1951**, **5**, 200). The appropriate volumes of liquids are introduced and the stoppers replaced. The apparatus is then turned 90° clockwise and equilibration is effected by shaking horizontally or by rocking about a small angle. After the phases have separated at rest, phase-interchange is brought about by slowly turning the apparatus anti-clockwise to restore it to the vertical position shown in the figure and then returning it as before to the horizontal or shaking position. Although extensive tests showed that this apparatus could not be relied upon implicitly for the procedure described in the present paper, it has a number of useful applications in procedures requiring systematic back-extractions, etc., where the use of taps is undesirable.

Experimental

Interchange Experiments.—Equilibration was carried out at 20° by shaking the appropriate mixtures mechanically in large stoppered Pyrex test-tubes; and centrifugation was employed to assist phase separation when necessary. Interchange of the appropriate 40-ml. aliquot of the aqueous phases (see above) was effected by means of calibrated pipettes. Both water and organic phases were pre-saturated with the second phase and the customary precautions necessary when working with dithizone were rigidly observed (cf. Irving, Andrew, and Risdon, *J.*, 1949, 539). The concentration of dithizone was determined absorptiometrically at 620 mμ in all cases, a Beckman Model DU Spectrophotometer with 1-cm. cells being used. An aliquot portion of the initial concentrated organic phase was suitably diluted before measurement (100-fold for carbon tetrachloride, 2-fold for *cyclo*hexane), but the absorbancy of the dilute organic extract in the second tube could be measured directly.

Carbon tetrachloride.

Absorbancy of initial solution ($\times 10^{-2}$)	0·557	0·581	0·501	0·501	0·501
Absorbancy of extract	0·117	0·157	0·106	0·109	0·098
Number of interchanges	3	4	3	3	3
$p_o \times 10^5$ (calc.)	6·6	6·75	6·6	6·8	6·1

cyclo*Hexane.*

Absorbancy of initial solution ($\times$ 0·5)	0·600	0·600	0·600	0·638	0·638	0·638
Absorbancy of extract	0·018	0·020	0·018	0·033	0·029	0·035
Number of interchanges	3	3	3	5	5	5
$p_o \times 10^4$	4·8	5·3	4·8	5·5	4·9	5·9

The Approach to Equilibrium from a Supersaturated Aqueous Phase.—5 ml. of a solution of dithizone in *cyclo*hexane were shaken in a large separating funnel with 500 ml. of water at 18° containing a few drops of concentrated ammonia solution. Dithizone was thus extracted into the aqueous phase as the yellow dithizonate ion, whence it was precipitated by the addition of 5 ml. of concentrated hydrochloric acid. After 15 minutes' shaking partition equilibrium had been established (this was confirmed by control experiments) and the greater part of the dithizone passed back into the organic solvent. After separation of the two phases (phase ratio 505/5) the concentration of dithizone in the organic layer was measured in terms of its absorbancy after suitable dilution, and that in the aqueous phase (approx. 0·1M-HCl) was obtained by equilibration with 5 ml. of fresh (pre-saturated) organic solvent and measuring the absorbancy of this extract.

cyclo*Hexane.*

Absorbancy of initial solution ($\times$ 0·2)	0·330	0·267	0·280	0·275	0·290
Absorbancy of organic extract	0·058	0·052	0·067	0·066	0·065
$p_o \times 10^4$	3·5	3·86	4·88	4·74	4·4

Benzene.

Absorbancy of initial solution ($\times 10^{-2}$)	0·147	0·147	0·143	0·595	0·575
Absorbancy of organic extract	0·022	0·017	0·016	0·096	0·068
$p_o \times 10^5$	1·47	1·14	1·11	1·63	1·17

The Distribution of Dithizone between Aqueous Buffers and Organic Solvents.—Distribution experiments were carried out as previously described (Irving *et al.*, *loc. cit.*) save that separating-funnels were replaced by stoppered Pyrex tubes wherever possible. Sodium hydroxide–boric acid buffers were employed in the case of benzene and carbon tetrachloride, potassium

hydroxide–potassium hydrogen phosphate buffers were used with *cyclo*hexane : sodium nitrate was present in each case to maintain a constant ionic strength of 0·14.

Benzene.						
pH	8·58	8·80	8·93	9·10	9·42	
Percentage extracted	20·2	32·1	40·4	50·6	69·8	
Carbon tetrachloride.						
pH	8·20	8·46	8·74	8·94	9·10	
Percentage extracted	16·0	32·2	46·8	57·0	66·5	
cyclo*Hexane.*						
pH	6·28	7·00	7·23	7·51	7·80	7·96
Percentage extracted	10·2	27·6	39·5	52·6	68·1	76·2

We are indebted to Mr. C. G. Tilley for making the measurements with the first two solvents. From plots of pH against $\log_{10}$ (percentage extracted) the values of $pH_{\frac{1}{2}}$ given in Table 3 were obtained by interpolation.

We thank Imperial Chemical Industries Limited for the loan of a Beckman Spectrophotometer, and one of us (C. F. B.) gratefully acknowledges the receipt of a maintenance grant from the Department of Scientific and Industrial Research.

THE INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, November 14th*, 1951.]

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220. *The Polymerizability of Methyl* α-tert.-*Butylacrylate.*

By J. W. C. CRAWFORD and (MISS) S. D. SWIFT.

Slow polymerization to low polymers, which appears to be generally characteristic of esters of higher α-alkylacrylic acids, may be due to steric hindrance by the α-alkyl groups in formation of the polymer chain. Degradative chain transfer on the monomer may be a contributory cause of the behaviour. In methyl α-*tert.*-butylacrylate, the magnitude of steric hindrance would probably be exceptionally high; the degradative chain-transfer reaction would not occur.

Methyl α-*tert.*-butylacrylate has been synthesized by dehydration of methyl tetramethyl-lactate. Attempts to produce polymers from the ester have been unsuccessful under a variety of conditions, and it is concluded that repulsion by the α-*tert.*-butyl group is sufficiently great to prevent polymerization.

IT appears to be generally the case that esters of α-alkylacrylic acids, when exposed to usual polymerizing conditions, very slowly yield polymers of low molecular weight. This has been observed on heating the methyl esters at 100° with benzoyl peroxide, for the cases where the α-alkyl group was ethyl, *n*- and *iso*-propyl, *n*-butyl, *n*- and *iso*-amyl, and cetyl. Methyl methacrylate is exceptional, since under such conditions it polymerizes readily and virtually completely to a macromolecular product.

The polymerization behaviour of the higher α-alkylacrylic esters can be a consequence of steric hindrance in chain formation, by the 1 : 1-substituents in the ethylene. Existence of this hindrance can be demonstrated by constructing sections of polymer with Stuart atom models, but conclusions from the model about the size of the repulsive forces can only be qualitative. The presence of strain as a result of steric hindrance is also shown in the Stuart model of sections of poly(methyl methacrylate), and Evans and Tyrrall (*J. Polymer Sci.*, 1947, **2**, 387) have found that the heat of polymerization of methyl methacrylate is 7·3 kcal./mole less than that of methyl acrylate, which can form an unstrained polymer. They have brought evidence that the lower heat of polymerization of the methacrylate is associated with steric hindrance in polymer chain formation by the α-methyl group.

Allyl acetate, when heated with benzoyl peroxide, slowly passes into a low polymer. Poly(allyl acetate) would be expected to be strain-free. To account for the behaviour of the acetate, Bartlett and Altschul (*J. Amer. Chem. Soc.*, 1945, **67**, 816) suggested that the growing poly(allyl acetate) radical reacts readily with the monomer, and the reaction is

terminated by union with hydrogen from the α-carbon atom of the monomer. The latter is thereby converted into a resonance-stabilized allylic radical incapable or barely capable of initiating further polymerization of allyl acetate. A similar "degradative chain transfer" seems feasible for α-alkylacrylic esters and would supplement steric hindrance in producing a tendency for slow polymerization to low polymers. Reaction of the polymer radical with the 1-hydrogen atom of the α-alkyl group in the monomer would end polymerization and convert the monomer into a radical (I) stabilized by resonance with (II).

$$\underset{\text{(I)}}{CH_2{:}\overset{CO_2Me}{\overset{|}{C}}{\cdot}CHR} \qquad \underset{\text{(II)}}{\cdot CH_2{\cdot}\overset{CO_2Me}{\overset{|}{C}}{:}CHR} \qquad \underset{\text{(III)}}{CH_2{:}\overset{CO_2Me}{\overset{|}{C}}{\cdot}CMe_2} \qquad \underset{\text{(IV)}}{CMe_2{\cdot}\overset{CO_2Me}{\overset{|}{C}}{\cdot}CH{:}\overset{CO_2Me}{\overset{|}{C}}{\cdot}CMe_2}$$

The ready polymerization of methyl methacrylate to a macromolecular product might be due to unimportance of the above transfer reaction in its case, because of the higher C–H bond energy in the α-methyl group than of the C–H bond energy of hydrogen combined with the 1-carbon atom in the higher α-alkyls. There are, however, no suitable bond-energy data from which to check this proposition. The values given by Roberts and Skinner (*Trans. Faraday Soc.*, 1949, **45**, 339) for R–H bond dissociation energies in ethane and propane suggest that the removal of hydrogen from the α-methyl group in methacrylate might require some 6 kcal./mole more than for removal of the 1-hydrogen atom from the α-ethyl group of α-ethylacrylate, but this conclusion would involve neglecting the effects of the adjacent vinyl and carboxymethyl group. No information is available for the activation energies of these processes.

The polymerizability of methyl α-*tert.*-butylacrylate (III) is of interest in this general connection. If steric hindrance is important in limiting the polymerizability of the α-alkylacrylic esters to macromolecular products, the α-*tert.*-butylacrylate should show the effects of this markedly, because of the bulkiness of the *tert.*-butyl group. Further, the degradative transfer reaction cannot occur in this case.

By using Stuart models, it was not found possible to construct model sections of poly(methyl α-*tert.*-butylacrylate), whether of head-to-tail, head-to-head, or tail-to-tail types, because of interference of the *tert.*-butyl groups with chain formation. It appeared indeed uncertain whether the ester would polymerize at all.

The polymerizability of methyl α-*tert.*-butyl acrylate was examined experimentally, material synthesized as described later being used.

The ester showed no visible signs of polymerization—passage to solid resin, deposition of polymer, or increase of viscosity—when heated at 100° with free-radical catalysts (benzoyl peroxide or azodi*iso*butyronitrile), or when exposed in borosilicate glass to ultra-violet radiation, with or without the presence in solution of benzoin photopolymerization catalyst. After prolonged exposure of the ester in glass to ultra-violet radiation at ordinary temperatures, its measured refractive index and viscosity were not significantly altered, no precipitate of polymer was obtained on addition of methanol or light petroleum, and the residue after evaporation of monomer was 0·04% of the weight of the latter.

In the absence of response to polymerizing conditions at ordinary or elevated temperatures, an attempt was made to polymerize methyl α-*tert.*-butylacrylate at a low temperature, at which, given effective activation, the free energy of the desired polymerization might be more favourable for its progress. Beaman (*J. Amer. Chem. Soc.*, 1948, **70**, 3115) has shown that methyl methacrylate is polymerized very rapidly and completely to a macromolecular product under conditions of anionic activation (sodium in liquid ammonia) at −80°. Application of Beaman's conditions to methyl α-*tert.*-butylacrylate produced only 0·8% of non-volatile residue, and this had a molecular weight little greater than that of the dimer (a head-to-head dimer could be formed, with some steric hindrance). It must be concluded from the experimental work that methyl α-*tert.*-butylacrylate is unable to furnish a polymer.

For poly*iso*butylene, Evans and Tyrrall (*loc. cit.*) were able to calculate a hypothetical value for the heat of polymerization in absence of strain, because of the existence of the strain-free head-to-tail dimer, 2 : 4 : 4-trimethylpent-1-ene. The value thus obtained, about 20 kcal./mole of monomer, was the same as that found experimentally in the

polymerization of monosubstituted ethylenes (*e.g.*, methyl acrylate) to unstrained polymers, and supported further the view that the lower value (12·8 kcal.) measured directly in the polymerization of *iso*butylene could be referred to steric hindrance of methyl groups. This treatment could not be followed in the present case, since it was apparent from the model that the possible head-to-tail dimer (IV) of methyl α-*tert.*-butylacrylate would be strained.

Methyl α-*tert.*-butylacrylate is readily hydrogenated to methyl α-*tert.*-butylpropionate (αββ-trimethybutyrate) at ordinary pressure and temperature, on use of palladium–barium sulphate catalyst. The boiling point of the propionate is only 2° lower than that of the acrylate, and separation of the two esters would not occur significantly under the conditions used for purification of the hydrogenation product. Mr. H. A. Willis has examined the infra-red absorption of this, and of pure methyl α-*tert.*-butylacrylate. The latter showed strong absorption at the C=C stretching frequency 1640 ν, corresponding closely to the same vibration for methyl methacrylate. This absorption was absent from the spectrum of the propionate. Examination of solutions of the acrylate of varying concentrations showed that the threshold of recognition of the C=C absorption would be at concentrations of acrylate of about 1%, from which it is concluded that the hydrogenation proceeds to the extent of 99% or better.

The heat of hydrogenation of methyl α-*tert.*-butylacrylate has been calculated, from the heats of combustion of acrylate and propionate, as 20·4 kcal./mole at 25°. This is lower than the calorimetrically measured heat of hydrogenation of methyl methacrylate—28·64 kcal./mole at 82° (Dollivier, Gresham, Kistiakowsky, Smith, and Vaughan *J. Amer. Chem. Soc.*, 1938, **60**, 440), but is liable to greater error. Although it may be that the heat of hydrogenation, and by inference the hypothetical strain-free heat of polymerization, is rather low, the inability to construct models of the polymer, because of interference by the α-*tert.*-butyl groups, suggests that steric hindrance is the primary cause of the non-polymerizability of methyl α-*tert.*-butylacrylate.

Experimental

Synthesis of Methyl α-tert.-*Butylacrylate.*—This followed the scheme

$$Me_3C{\cdot}CO{\cdot}CH_3 \longrightarrow Me_3C{\cdot}CO{\cdot}CO_2H \longrightarrow Me_3C{\cdot}CO{\cdot}CO_2Me \xrightarrow{MgMeI} Me_3C{\cdot}CMe(OH){\cdot}CO_2Me \xrightarrow{-H_2O} (III)$$

Trimethylpyruvic acid and methyl ester. The acid was prepared by oxidizing pinacone with potassium permanganate (Richard, *Ann. Chim.*, 1910, **21**, 360). Richard's claim of an 80% yield of distilled acid was substantiated with 80-g. batches of ketone, provided that the alkaline oxidation product, filtered from manganese dioxide, was neutralized to litmus with hydrochloric acid before concentration and liberation of the trimethylpyruvic acid : neglect of neutralization resulted in yields of 50—60%. The methyl ester, prepared as described by Richard, had b. p. 44—45°/12 mm. (yield, 82%).

Methyl tetramethyl-lactate. Methyl trimethylpyruvate (81 g., 0·56 mole), in an equal volume of ether, was added to a solution of methylmagnesium iodide [from magnesium, 27·3 g. (1·14 g.-atom), and methyl iodide, 160 g.] in ether (500 c.c.), the reaction mixture being stirred, and cooled to below −10° during the addition. Vigorous reaction and formation of a precipitate, which at once redissolved, accompanied addition of each drop of ester. 10 Minutes after addition was complete, the mixture was poured on 900 g. of cracked ice, magnesia dissolved by addition of hydrochloric acid, the ethereal layer washed four times with water and dried (Na_2SO_4), the solvent removed, and the residue fractionated through a 9-inch Vigreux column. After a few drops of forerun, almost all distilled at 64—64·5°/14 mm. (yield 73 g., 81%). Use of an equimolar amount of Grignard reagent gave yields around 50%.

The redistilled ester had b. p. 58·5°/10 mm., n_D^{20} 1·4275, d_4^{20} 0·9801, $[R_L]_D$ 42·00 (Calc.: 42·32); when cooled to −80°, it formed a glass [Found : C, 60·1; H, 9·9%; *M* (cryoscopic in benzene), 158. Calc. for $C_8H_{16}O_3$: C, 60·0; H, 10·0%; *M*, 160]. The ester is only slowly hydrolyzed by boiling 0·5N-alcoholic potash (Sap. val. : 2 hours' reflux, 286·3; 4 hours' reflux, 345·2; 8 hours' reflux, 352·3. Calc. : 350).

Methyl α-tert.-*butylacrylate.* Methyl tetramethyl-lactate (75 g., 0·47 mole), phosphoric oxide (77 g., 0·54 mole), and dimethylaniline (77 g., 0·64 mole) were heated for 22 hours on the water-bath. The product was distilled from a metal-bath, a simple distillation head being used,

at such a rate that the vapour temperature did not exceed 170°. This occupied 1—2 hours. The distillate (88 g.) was washed four times with dilute hydrochloric acid, twice with water, and dried ($CaCl_2$), and the product (60 g.) fractionally distilled at atmospheric pressure, a 6-inch precision column of 12 plates' rating (Dixon, *J. Soc. Chem. Ind.*, 1949, **68**, 299) being used. After a moist fore-run (4 g.) had passed over, methyl α-*tert.*-butylacrylate was collected at 146—149°/755 mm. (29 g., 40·6%). The residue was unchanged methyl tetramethyl-lactate, containing some butylacrylate. Mixed with fresh lactate, it was used in a subsequent preparation of butylacrylate, the yield being the same as with pure lactate.

On redistillation, *methyl* α-tert.-*butylacrylate* had b. p. 147—147·4°/757 mm., m. p. −36°, n_4^{20} 1·4273, d_4^{20} 0·9126, $[R_L]_D$ 40·00 (Calc.: 40·33) [Found: C, 67·2; H, 10·0%; *M* (cryoscopic in benzene), 139. Calc. for $C_8H_{14}O_2$: C, 67·6; H, 9·8%; *M*, 142]; like methyl tetramethyl-lactate, it is only slowly hydrolyzed by boiling alcoholic potash (Sap. val.: 2 hours' reflux, 330·1; 4 hours', 357; 8 hours' 383; 16 hours', 397. Calc., 396).

Polymerizability.—(*a*) 1-g. samples of the ester, containing in solution 1% of benzoyl peroxide or azodi*iso*butyronitrile $[CMe_2{\cdot}C(CN){\cdot}N:]_2$, were sealed under nitrogen in glass tubes and heated at 100° for 72 and 118 hours, respectively. No visual evidence of polymerization was obtained. Similar results followed exposure of ester, with or without 0·1% of benzoin in solution, and sealed under nitrogen in Pyrex-glass tubes, to the radiation from a 250-watt Mazda compact-source mercury-in-silica lamp (type ME/D) at 12 in. distance.

(*b*) The ester used had been prepared 4 days previously, and stored meanwhile in the dark at ordinary temperature. Through 6 ml. of this, in a Pyrex tube (13 mm. outside diam.), a stream of oxygen-free nitrogen was passed for 5 minutes, the ester frozen, and the tube sealed off with exclusion of air. The tube was placed vertically in a cold water-jacket of transparent silica (internal diam. 25 mm.), and exposed to the radiation from the Mazda lamp at 10 inches for 88½ hours. Values of refractive index and absolute viscosity found for the ester before and after the above irradiation were, respectively: n_D^{20} 1·4273, 1·4274; η^{20} 1·24, 1·26 c.p. The irradiated ester gave clear solutions when mixed with 4 volumes of methanol or light petroleum (b. p. 100—120°). The irradiated ester was evaporated in a basin in an oven at 110°, heating being continued for 15 minutes after disappearance of liquid (the limited heating period being to minimize effects of possible depolymerization). The residue amounted to 0·04% of the weight of monomer, and was a tacky invisible film, removed by cold chloroform. A sample of the original ester, now about 15 days old, gave also 0·04% of residue when subjected to the same evaporation procedure; the residue in either case might have been an autoxidation product. In a control irradiation under the same conditions, methyl methacrylate was syrupy after 10 hours.

(*c*) Sodium (0·1 g.), dissolved in liquid ammonia (25 ml.), was cooled to −80° in solid carbon dioxide–methanol, and methyl α-*tert.*-butylacrylate (4 g.) added. The blue sodium solution was immediately decolorized. After 30 minutes at −80°, ammonium chloride (0·5 g.) was added, and ammonia removed by allowing the mixture to warm to room temperature. The residue, a mixture of liquid and white solid, was treated with water (20 ml.), which dissolved all the solids. The sharply demarcated ester layer was separated, washed three times with water, and dried (Na_2SO_4). The dried ester was evaporated in a basin in an oven at 110° for 15 minutes after disappearance of liquid, and left 0·8% of residue; continuation of heating until constant weight was reached left 0·5% of residue. This was a light brown gum [*M* (Rast), 327. Calc. for dimeric methyl α-*tert.*-butylacrylate: *M*, 284].

Hydrogenation of Methyl α-tert.-*Butylacrylate.*—Methyl α-*tert.*-butylacrylate (20 g., 0·14 mole), dissolved in methanol (80 g.), was hydrogenated in a shaker in presence of 5% palladium–barium sulphate (5 g.) at an initial temperature of 24°. After saturation, the liquid was filtered from catalyst, and methanol removed by fractional distillation through an 18-inch Vigreux column with 10 : 1 reflux ratio. The slightly moist residue was fractionated at atmospheric pressure through a 6-inch Dixon column (*loc. cit.*). After removal of further methanol, and moist ester (1 g.), methyl 1-*tert.*-butylpropionate (13 g., 64%) was collected at 145—146°/758·5 mm.; it had n_D^{20} 1·4122, d_4^{20} 0·8809, $[R_L]_D$ 40·40 (Calc.: 40·80).

Heats of Combustion (1 *atm.*).—Methyl α-*tert.*-butylacrylate: 21·0°, 1132·8; 21·2°, 1132·4; 27·5°, 1127·7; 27·7°, 1128·3 kcal./mole; linear interpolation gave 1129·9 kcal./mole at 25°. Methyl α-*tert.*-butylpropionate: 20·0°, 1177·5; 22·3°, 1177·7 kcal./mole; linear extrapolation gave 1177·9 kcal./mole at 25°.

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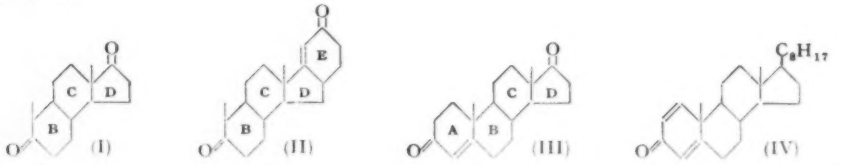
221. *Experiments on the Synthesis of Substances related to the Sterols. Part L. The A→BCD Route. Part III.**

By A. R. Pinder and Sir Robert Robinson.

The oily, tricyclic ketone obtained by Inhoffen and Huang-Minlon (*Ber.*, 1939, **72**, 1686) by the ozonolysis of cholesta-1 : 4-dien-3-one has been obtained crystalline (m. p. 52°), and an improved method of preparation devised. The ketone has been converted into the Windaus keto-acid (VII) which has already been converted by way of cholestenone into cholesterol.

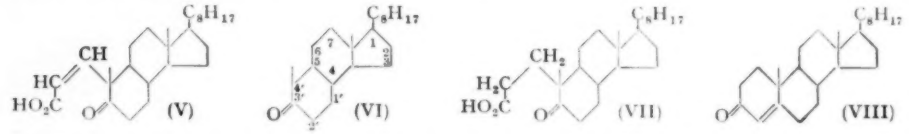
Some model experiments with 1-methyl-*cis*-2-decalone and 1-methyl-*trans*-2-decalone are described, and a new synthesis of the latter ketone is reported. A striking contrast in the reactivity of these ketones was encountered in connexion with their conversion into hydrophenanthrene derivatives.

In Part XLI (Martin and Robinson *J.*, 1943, 491) and Part XLIX (*idem*, *J.*, 1949, 1866) an attempt to add ring A to the synthetic BCD tricyclic diketone (I), using the Mannich-base methiodide reaction, was described. The product was shown to be a mixture of stereoisomerides of the BCDE tetracyclic ketone (II), rather than of stereoisomeric androstenediones (III).



The objective of the present experiments was to achieve the addition of ring A to a BCD-tricyclic substance which latter, it was hoped, might eventually be linked with the BCD synthetic series. The first stage of this programme has been realised and a brief preliminary announcement has been made (*Nature*, 1951, **167**, 484).

In 1938, Inhoffen and Huang-Minlon (*Ber.*, 1938, **71**, 1720) showed that the ozonolysis of cholesta-1 : 4-dien-3-one (IV) gave an unsaturated acid (V), ring A in the dienone being ruptured. Subsequently, the same authors found that the acid was accompanied by a neutral product, considered to be the BCD-tricyclic ketone (VI) (*Ber.*, 1939, **72**, 1686), which was oily but formed a crystalline semicarbazone.



We have re-investigated the formation of this neutral ketone and have confirmed its assumed relation to cholestenone and its structure as 1-(1 : 5-dimethylhexyl)perhydro-3′-keto-7*a* : 4′-dimethyl-4 : 5-benzindene (VI).† After model experiments with simple 2-decalones, the ketone was successfully converted into the keto-acid (VII), obtained as a degradation product of cholestenone by Windaus (*Ber.*, 1906, **39**, 2008). This acid has recently been converted into cholest-4-en-3-one (VIII) (Turner, *J. Amer. Chem. Soc.*,

* Part XLIX and Part II, *J.*, 1949, 1866.

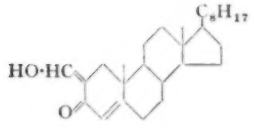
† This name is cumbrous and we suggest that cholestane stripped of the four methylene groups of ring A could be termed *des-A-cholestane*. It will be simplest in this case to retain the cholestane numbering system and Inhoffen's ketone becomes des-A-cholestan-5-one.

This system is especially useful for derivatives; the substance itself can still be termed the Inhoffen ketone.

Furthermore, the des-names specify the stereochemistry which is neglected in the systematic name used above and added in the Experimental section.

(" des " is preferred to the customary British " de " in this usage so as to avoid ambiguity in speech; *e.g.*, des-D is preferable in speech to de-D.)

1950, **72**, 579), which has in turn been converted into cholesterol (Dauben and Eastham, *ibid.*, p. 2305; Birch, *J.*, 1950, 2325).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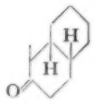
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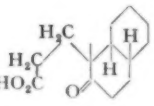
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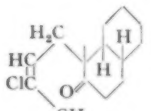
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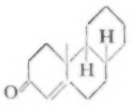

(XIII)

Cholesta-1 : 4-dien-3-one (IV) was prepared by dehydrobromination of 2 : 4-dibromocholestan-3-one (Wilds and Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1712). We have found that by starting with the pure dibromo-ketone yields of 70% of the pure dienone (m. p. 111—111·5°) could be obtained without adopting the tedious chromatographic purification described by these authors. Ozonolysis of the dienone gave a neutral gum, which when purified by adsorption on alumina gave a 15% yield of the crystalline Inhoffen ketone, m. p. 52°. The ketone was first obtained crystalline, m. p. 42°, in this laboratory by Dr. R. P. A. Sneeden (Thesis, Oxford, 1950).

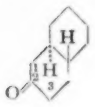
During attempts to improve the preparation it was found that oxidation of the dienone (IV) by permanganate also afforded the ketone, though in smaller yield. A more convenient method was the permanganate oxidation of 2-hydroxymethylenecholest-4-en-3-one (IX), obtained by the condensation of cholestenone and ethyl formate with the help of sodium methoxide. The idea here was to sensitise the ring-A carbon atoms by progressive enolisation.

With the object of finding the best method of adding ring A to the Inhoffen ketone, the behaviour of two model ketones in standard reactions was studied. It was realised that 1-methyl-*cis*-2-decalone (X) * was not a suitable model, because of the *cis*-decalin system present, yet it was felt that it would be of interest to study its reactions, as it was comparatively readily available (Robinson and Weygand, *J.*, 1941, 391). The addition of acrylonitrile to this ketone (cf. Bruson, "Organic Reactions," Vol. V, p. 79, New York, 1949) gave, after hydrolysis, a monocarboxylic acid in high yield. The structure (XI) has been assigned to this acid, since *cis*-2-decalones are known to be more reactive at $C_{(1)}$ than at $C_{(3)}$ (Butenandt and Wolff, *Ber.*, 1935, **68**, 2091). Further, the reactivity of acrylonitrile is such that substitution usually occurs at all reactive positions in the ketone (Bruson, *loc. cit.*); the monocarboxylic character of the only acid isolated from the reaction suggests that the side-chain is at $C_{(1)}$. This is in harmony with Robinson and Weygand's observation (*loc. cit.*) that condensation of 1-methyl-*cis*-2-decalone with diethylaminobutanone methiodide gave the reduced phenanthrene ketone (XIII) exclusively, none of the isomeric ketone with an anthracene skeleton being obtained. Further, we have observed that condensation of the decalone with 1 : 3-dichlorobut-2-ene (cf. Wichterle, *Coll. Czech. Chem. Comm.*, 1947, **12**, 93; 1948, **13**, 300; Prelog, Barman, and Zimmermann, *Helv. Chim. Acta*, 1949, **32**, 1284) gives 1-(3-chlorobut-2-enyl)-1-methyl-*cis*-2-decalone (XII), which cyclises smoothly in sulphuric acid to give the tricyclic ketone (XIII), identical with Robinson and Weygand's product.

A better model ketone was 1-methyl-*trans*-2-decalone (XVII), which Rao and Kuppuswamy (*J. Annamalai Univ.*, 1937, **7**, 22) claim to have prepared by direct methylation of *trans*-2-decalone (XIV) with sodamide and methyl iodide. It is, however, doubtful if their product contained any of the desired ketone, in view of the greater reactivity of *trans*-2-decalone at $C_{(3)}$ (Butenandt and Wolff, *loc. cit.*). English and Cavaglieri (*J. Amer. Chem. Soc.*, 1943, **65**, 1088) prepared the ketone by a series of steps from *trans*-1-decalone, the over-all yield being 20%. We have synthesised the ketone from the accessible *trans*-2-decalol (m. p. 75°), oxidation of which by means of chromic acid gave *trans*-2-decalone (XIV) (Hückel, *Annalen*, 1925, **441**, 19). Necessary blockage of the 3-position in *trans*-

* In this and other decalin formulæ, the sterol convention of full and broken lines is used for the ring-junction hydrogen atoms. It is not however intended to specify the configuration at other positions of the decalin rings.

2-decalone was effected by condensation with ethyl formate, giving 3-hydroxymethylene-*trans*-2-decalone (XV), which condensed with methylaniline (cf. Birch and Robinson, *J.*, 1944, 501) furnishing 3-methylanilinomethylene-*trans*-2-decalone (XVI). Methylation of this compound, followed by removal of the blocking group and prolonged treatment with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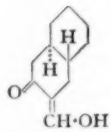
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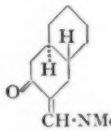
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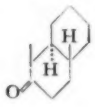
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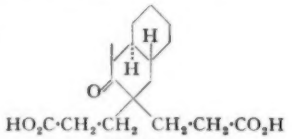
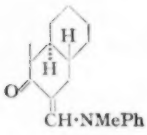

(XVIII)

alkali (cf. Hückel, *loc. cit.*), gave a stereochemically homogeneous ketone, one of the two forms of 1-methyl-*trans*-2-decalone (XVII). The product was identical with that of English and Cavaglieri (*loc. cit.*). We are grateful to Professor J. English, of Yale University, for providing specimens for comparison. The identity of these products provides formal proof that, in its reaction with ethyl formate, *trans*-2-decalone is attacked at $C_{(3)}$.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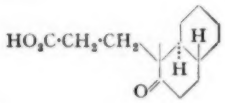
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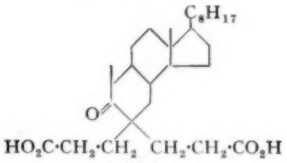
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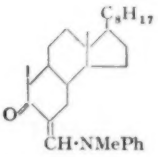
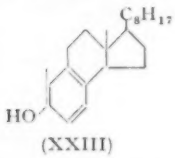

(XXII)

The reaction of 1-methyl-*trans*-2-decalone with acrylonitrile (1 mol.), followed by hydrolysis, gave a 40% yield of a dicarboxylic acid $C_{11}H_{16}O(CH_2{\cdot}CH_2{\cdot}CO_2H)_2$. We have formulated this acid as (XVIII), since the parent ketone is more reactive at $C_{(3)}$ than at $C_{(1)}$. This behaviour is in marked contrast to that of 1-methyl-*cis*-2-decalone. 1-Methyl-*trans*-2-decalone was reconverted into 1-methyl-3-methylanilinomethylene-*trans*-2-decalone (XIX; already made in a less homogeneous form by methylation of XVI), which reacted with acrylonitrile to give, after hydrolysis and elimination of the methylanilinomethylene group, 1-2′-carboxyethyl-1-methyl-*trans*-2-decalone (XX), in 10% yield.

Turning to the Inhoffen ketone, we attempted unsuccessfully to convert the ketone directly into cholestenone (VIII) by condensation with diethylaminobutanone methiodide, or with 1 : 3-dichlorobut-2-ene. Reaction of the ketone with acrylonitrile gave, after hydrolysis, a dicarboxylic acid, formulated by analogy as (XXI). Blockage of the 7-position in the ketone by the usual technique gave the 7-methylanilinomethylene ketone (XXII). The reaction of the latter with acrylonitrile, followed by hydrolysis and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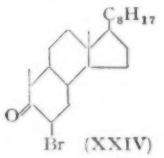
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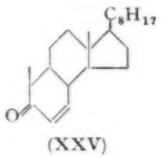
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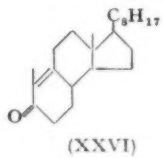
(XXVI)

removal of the blocking group, gave a small yield of a crystalline, monocarboxylic acid, m. p. 154°, which was identical in all respects with an authentic specimen of the Windaus keto-acid (VII), prepared by the ozonolysis of cholest-4-en-3-one (Turner, *loc. cit.*). We are grateful to Mrs. D. M. Hodgkin, who kindly carried out *X*-ray crystallographic investigations of the two specimens and reported that they were identical. The chain of reactions whereby Inhoffen ketone may be transformed into cholesterol is now complete.

We are now attempting the dehydrogenation of ring B of the Inhoffen ketone, the objective being the phenol (XXIII). Direct dehydrogenation of the ketone with sulphur, selenium, or palladium–charcoal has not given a phenolic product, owing to elimination of

the oxygen atom. Bromination of the ketone with an excess of bromine gave a monobromo-ketone, dehydrobromination of which with collidine gave an enone whose ultraviolet absorption spectrum showed $\lambda_{max.}$ 235 mμ (ε_{molar} = 15 850). The product is evidently des-A-cholest-6-en-5-one (XXV) [$\lambda_{max.}$ (calc.) 227 mμ] rather than (XXVI) [$\lambda_{max.}$ (calc.) 254 mμ], and the intermediate bromo-ketone is 6-bromodes-A-cholesten-5-one (XXIV). Efforts to dehydrogenate (XXV) to (XXIII) have not so far proved successful, nor has it been found possible to introduce a second bromine atom into (XXIV) at $C_{(10)}$.

Experimental

(Alumina was Type A from Messrs. Peter Spence & Co.)

1-*Methyl*-cis-2-*decalone* (X).—Methylenebis-2-naphthol (Fries and Hübner, *Ber.*, 1906, **39**, 440) was reduced to 1-methyl-2-naphthol (Cornforth, Cornforth, and Robinson, *J.*, 1942, 682) and then to stereoisomeric 1-methyl-*cis*-2-decalols (Robinson and Weygand, *loc. cit.*). Chromic acid oxidation of the decalol gave 1-methyl-2-decalone (one of the two possible *cis*-forms; Robinson and Weygand, *loc. cit.*). The ketone distilled at 140—145° (bath)/12 mm. and gave a semicarbazone, elongated colourless prisms, m. p. 183—184° (Found: N, 19·0. Calc. for $C_{12}H_{21}ON_3$: N, 18·8%). Robinson and Weygand (*loc. cit.*) give m. p. 185—191°.

1-2′-*Carboxyethyl*-1-*methyl*-cis-2-*decalone* (XI).—"Triton B" (1 c.c.; commercial 20% aqueous benzyltrimethylammonium hydroxide; Rohm and Haas Inc.), followed by acrylonitrile (0·38 g., 1 mol.), was added with shaking and cooling to a solution of 1-methyl-*cis*-2-decalone (1·2 g.) in dioxan (5 c.c.). After 48 hours at room temperature the solution was acidified and the dioxan evaporated *in vacuo*. The residual oil, isolated with ether, was heated under reflux for 20 hours with aqueous potassium hydroxide (30 c.c. of 20%). The cooled solution was diluted with water, and neutral matter extracted with ether. Acidification and ether-extraction of the alkaline solution gave a colourless gum (1·0 g.) which soon crystallised. 1-2′-*Carboxyethyl*-1-*methyl*-cis-2-*decalone* crystallised from dilute acetic acid in clusters of small, colourless, prisms m. p. 116° (Found: C, 70·1; H, 9·2%; equiv., 236·0. $C_{14}H_{22}O_3$ requires C, 70·6; H, 9·2%; equiv. 238).

$\Delta^{1(11)}$-*Dodecahydro*-2-*keto*-12-*methylphenanthrene* (XIII).—A solution of 1-methyl-*cis*-2-decalone (4·15 g.; 1 mol.) in dry ether (25 c.c.) was added to a cooled ethereal solution of triphenylmethylsodium (190 c.c. of 0·13M), under nitrogen. After 30 minutes a solution of 1 : 3-dichlorobut-2-ene (3·2 g., 1 mol.) in dry ether (20 c.c.) was introduced with cooling and swirling. Next day the mixture was refluxed on the steam-bath for 3 hours; some sodium chloride then separated. The cooled mixture was poured into water, and the organic layer separated, dried, and distilled. The residual syrup was mixed with a little methanol and kept at 0° for several hours, after which crystals of triphenylmethane were collected and washed with cold methanol. Evaporation of the filtrate left an oil which was distilled. The fore-run, b. p. 120—150° (bath)/0·09 mm. (3·1 g.), was mainly unchanged ketone. The next fraction, b. p. 150—170° (bath)/0·09 mm. (1·7 g.), was 1-(3-chlorobut-2-enyl)-1-methyl-*cis*-2-decalone (XII). Sulphuric acid (4 c.c.) was added with cooling and the mixture kept until the evolution of hydrogen chloride ceased (*ca.* 3 hours). Ice was added and the product isolated by means of ether. The yellow gum (1·48 g.) which contained some triphenylmethane was taken up in light petroleum (b. p. 40—60°), and the solution passed through an alumina column. A pale yellow (in ultra-violet light) band was obtained uppermost; elutions with ether and methanol gave $\Delta^{1(11)}$-*dodecahydro*-2-*keto*-12-*methylphenanthrene* as a pale yellow oil (0·3 g.), b. p. 165—170° (bath)/0·08 mm. (Found: C, 82·3; H, 10·0. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%). The ultra-violet absorption spectrum showed a maximum at 245 mμ (log ε_{molar} = 3·6).

The semicarbazone separated from absolute alcohol in small needles, m. p. 224—225° (decomp.) (Found: C, 70·2; H, 8·9; N, 14·4. Calc. for $C_{16}H_{25}ON_3$: C, 69·8; H, 9·1; N, 15·3%). Robinson and Weygand (*loc. cit.*) give m. p. 225—230° (decomp.).

trans-2-*Decalone* (XIV).—Oxidation of commercially available *trans*-2-decalol (m. p. 75°) with chromic acid gave *trans*-2-decalone in 75% yield (Hückel, *Annalen*, 1925, **441**, 19), purified through its bisulphite compound. The ketone distilled at 128—129°/23 mm.

3-*Methylanilinomethylene*-trans-2-*decalone* (XVI).—Alcohol-free sodium methoxide (from 1·5 g. of sodium) was suspended in dry ether (65 c.c.) and powdered as possible. Ethyl formate (5·0 g.) was added with shaking and cooling, followed by *trans*-2-decalone (5·0 g.) in dry ether (10 c.c.), dropwise. Next morning, the mixture was decomposed with ice, and the organic layer separated and washed with dilute alkali. Acidification of the combined alkaline solutions furnished a yellow oil which was taken up in ether. Evaporation of the dried ethereal

solution gave 3-hydroxymethylene-*trans*-2-decalone (XV) as a yellow syrup (5·8 g.) which was not purified; it gave a purple ferric reaction.

A mixture of the hydroxymethylene-ketone (11·9 g.), freshly distilled methylaniline (7·5 g.), and benzene (100 c.c.) was distilled slowly from the steam-bath during 2 hours (cf. Birch and Robinson, *J.*, 1944, 501), the remaining benzene being removed *in vacuo*. The residual orange-red oil (18·0 g.) crystallised entirely when kept. 3-*Methylanilinomethylene*-trans-2-*decalone* separated from light petroleum (b. p. 60—80°) in yellow, elongated prisms, m. p. 87° (Found: C, 80·2; H, 8·4. $C_{18}H_{23}ON$ requires C, 80·3; H, 8·6%).

1-*Methyl*-2-*decalone* (trans-*forms*) (XVII).—A solution of 3-methylanilinomethylene-*trans*-2-decalone (9·0 g., 1 mol.) in dry ether (120 c.c.) was added to a cooled ethereal solution of triphenylmethylsodium (280 c.c. of 0·12M), under a nitrogen atmosphere during 15 minutes, with swirling; methyl iodide (10 g., 2·1 mol.) in dry ether 25 c.c. was then introduced. The mixture was refluxed gently on the steam-bath for 2 hours, then poured into water, and the organic layer separated, dried, and evaporated. The oily residue was refluxed for 30 minutes with 10% hydrochloric acid (200 c.c.), and the mixture cooled and extracted with ether. The ethereal solution was extracted several times with cold, dilute alkali, and the combined alkaline solutions were acidified. The oil liberated was taken up in ether, the ether evaporated, and the residue hydrolysed by boiling it with sodium hydroxide solution (60 c.c. of 15%) for 30 minutes. The cooled mixture was extracted several times with ether. Evaporation of the solvent gave a mixture of the two forms of 1-methyl-*trans*-2-decalone, which distilled at 110—113°/10 mm. (3·9 g.) (Found: C, 79·3; H, 11·0. Calc. for $C_{11}H_{18}O$: C, 79·5; H, 10·8%).

The 2 : 4-dinitrophenylhydrazone separated from alcohol in clusters of orange needles, m. p. 171—172° with previous softening at 165° (Found: C, 58·8; H, 6·3; N, 15·9. Calc. for $C_{17}H_{22}O_4N_4$: C, 58·9; H, 6·3; N, 16·2%). The semicarbazone crystallised from alcohol in colourless needles, m. p. 198—199° with previous softening at 195° (Found: C, 64·4; H, 9·3. Calc. for $C_{12}H_{21}ON_3$: C, 64·6; H, 9·4%).

By boiling the product (3·5 g.) under reflux for 16 hours with 4N-potassium hydroxide (60 c.c.), it was converted into a stereochemically homogeneous ketone, one of the two forms of 1-methyl-*trans*-2-decalone, isolated with ether. The ketone distilled at 110°/11 mm. (Found: C, 79·1; H, 11·1. Calc. for $C_{11}H_{18}O$: C, 79·5; H, 10·8%).

The 2 : 4-dinitrophenylhydrazone separated from alcohol in orange needles, m. p. 171—172° with no previous softening. The semicarbazone separated from alcohol in colourless prisms, m. p. 204—205°, with no previous softening. These two derivatives showed no m. p. depression on admixture respectively with specimens kindly supplied by Professor J. English, of Yale University (English and Cavaglieri, *loc. cit.*).

3 : 3-*Bis*-2′-*carboxyethyl*-1-*methyl*-trans-2-*decalone* (XVIII).—The reaction of 1-methyl-*trans*-2-decalone (2·0 g.) (stereochemically homogeneous) in dioxan (10 c.c.) with acrylonitrile (0·64 g.), in the presence of " Triton B " under the usual conditions, furnished an oil which on hydrolysis gave an acidic gum (1·0 g.) which crystallised readily. 3 : 3-*Bis*-2′-*carboxyethyl*-1-*methyl*-trans-2-*decalone* separated from acetone in colourless rods, m. p. 192° (Found: C, 65·7; H, 8·1%; equiv., 153·2. $C_{17}H_{26}O_5$ requires C, 65·8; H, 8·4%; equiv., 155).

1-*Methyl*-3-*methylanilinomethylene*-trans-2-*decalone* (XIX).—This compound, an intermediate in the conversion of 3-methylanilinomethylene-*trans*-2-decalone (XVI) into 1-methyl-*trans*-2-decalone, was made in a pure state from the latter substance. Condensation of 1-methyl-*trans*-2-decalone (3·3 g.) with ethyl formate (3·0 g.) in the presence of sodium methoxide (from 1·0 g. of sodium) under the usual conditions furnished 3-hydroxymethylene-1-methyl-*trans*-2-decalone (3·8 g.) as a syrup. This was heated on the steam-bath with benzene (40 c.c.) and methylaniline (2·2 g.) for 2 hours, and the solvent slowly distilled. 1-*Methyl*-3-*methylanilinomethylene*-trans-2-*decalone*, isolated in the usual manner, separated from light petroleum (b. p. 60—80°) in pale yellow prisms (4·0 g.), m. p. 105° (Found: C, 80·8; H, 9·0. $C_{19}H_{25}ON$ requires C, 80·6; H, 8·8%).

1-2′-*Carboxyethyl*-1-*methyl*-trans-2-*decalone* (XX).—" Triton B " (3 c.c.), followed by acrylonitrile (0·72 g.), was added with cooling to a solution of 1-methyl-3-methylanilinomethylene-*trans*-2-decalone (3·5 g.) in dioxan (20 c.c.). After 60 hours at room temperature, the solution was acidified and the dioxan evaporated *in vacuo*. The oil which separated was isolated by means of ether and heated under reflux for 30 minutes with hydrochloric acid (60 c.c. of 10%). The solution was cooled and the organic material isolated with ether and heated under reflux for 20 hours with aqueous potassium hydroxide (80 c.c. of 20%). The cooled, diluted solution was freed from neutral matter with ether and acidified. The liberated acid was taken up in ether; evaporation gave a gum (0·4 g.) which crystallised on trituration with acetone.

1-2′-*Carboxyethyl*-1-*methyl*-trans-2-*decalone* separated from acetone in glistening, elongated prisms, m. p. 139—140° (Found: C, 70·7; H, 9·2%; equiv., 238·2. $C_{14}H_{22}O_3$ requires C, 70·6; H, 9·2%; equiv., 238).

An uncrystallisable gum (0·2 g.) obtained from the acetone mother-liquors may consist in part of the epimeric form of the acid.

Cholesta-1 : 4-*dien*-3-*one* (IV).—The following modification of the procedure of Wilds and Djerassi (*loc. cit.*) gave consistent yields of 70% of pure material, m. p. 111—111·5°. A solution of pure 2 : 4-dibromocholestan-3-one (5 g.; m. p. 193—194°; Wilds and Djerassi, *loc. cit.*) in purified collidine (20 c.c.) was heated under reflux at 185° (bath-temp.) for 80 minutes. The cooled solution was filtered and the collidine hydrobromide (theoretical yield) thoroughly washed with ether. The ether and excess of collidine were evaporated, finally *in vacuo*, and the dark, oily residue taken up in ether. The ethereal solution was washed in turn with dilute acid, sodium hydrogen carbonate solution, and water, then dried, and the solvent was evaporated. The brown residual oil crystallised readily; crystallisation from a small volume of light petroleum (b. p. 40—60°) gave cholesta-1 : 4-dien-3-one as pale fawn-coloured rhombs, m. p. 111—111·5° (2·5 g., 71%). Wilds and Djerassi (*loc. cit.*) give m. p. 110—112°. The 2 : 4-dinitrophenylhydrazone separated from ethyl acetate in minute, deep-red prisms, m. p. 184—185° (Found: C, 70·2; H, 8·2. Calc. for $C_{33}H_{46}O_4N_4$: C, 70·5; H, 8·2%). Djerassi (*J. Amer. Chem. Soc.*, 1949, **71**, 1008) gives m. p. 183—184°.

1-(1 : 5-*Dimethylhexyl*)*perhydro*-3′-*keto*-7a : 4′-*dimethyl*-4 : 5-*benzindene* (*Inhoffen's ketone*; *des*-A-*cholestan*-5-*one*) (VI).—The following modification of Inhoffen and Huang-Minlon's procedure (*loc. cit.*) was employed. A solution of cholesta-1 : 4-dien-3-one (3 g.) in acetic acid (10 c.c.) was ozonised for 24 hours at room temperature. The solution was diluted with water (30 c.c.) and refluxed for 30 minutes. The cooled, oily suspension was diluted with water and extracted twice with ether. The ethereal solution was thoroughly extracted with 5% aqueous potassium hydroxide, washed with water, and dried. Evaporation of the ether gave a pale yellow gum (0·8 g.) which did not crystallise. It was dissolved in light petroleum (b. p. 40—60°) and adsorbed on a 10-cm. column of alumina (*ca.* 10 g.). The ketone formed a pale-blue band, easily visible in ultra-violet light, and easily eluted with 1 : 1 light petroleum (b. p. 40—60°)–benzene. Evaporation of the eluate gave an almost colourless oil (0·4 g.) which crystallised entirely, m. p. 51—52°. *Des*-A-*cholestan*-5-*one* separated from light petroleum (b. p. 40—60°), with ice-cooling, in fine, white prisms, m. p. 52°, $[\alpha]_D^{18}$ +14·2° in chloroform (Found: C, 83·4; H, 12·1. $C_{23}H_{40}O$ requires C, 83·1; H, 12·1%). The semicarbazone separated from ethanol in minute, elongated prisms, m. p. 225—226° (decomp.). Inhoffen and Huang-Minlon (*loc. cit.*) give m. p. 224—225° (decomp.). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in clusters of orange-yellow prisms, m. p. 179° (Found: C, 68·0; H, 8·7. $C_{29}H_{44}O_4N_4$ requires C, 68·0; H, 8·6%).

Acidification of the alkaline washings gave des-A-cholestan-5-one-10-β-acrylic acid (V) (2·1 g.) as a gum which crystallised readily. The acid separated from acetone in colourless needles, m. p. 206—207° (Found: equiv., 400·1. Calc. for a monobasic acid $C_{26}H_{42}O_3$: equiv., 402). Inhoffen and Huang-Minlon (*loc. cit.*) give m. p. 207—207·5°.

Alternative Methods of Preparation of the Inhoffen Ketone.—(a) *Permanganate oxidation of cholesta*-1 : 4-*dien*-3-*one*. A solution of cholestadienone (3 g.) in acetone (100 c.c.) was stirred at 0° during the addition of powdered potassium permanganate (9·0 g.) over 15 minutes. Stirring was continued for 2 hours, after which the mixture was filtered. The residue was dried at the room temperature for several hours, then suspended in water, and sulphur dioxide passed through, with cooling. The clear solution was acidified and extracted several times with ether. Evaporation of the solvent gave an acidic gum (2·9 g.) which was heated at 170—180° for 30 minutes. The cooled product was taken up in ether, and the solution extracted with dilute alkali. Evaporation of the ethereal solution left a pale yellow gum (0·3 g.) from which the Inhoffen ketone (0·2 g.; m. p. 52°) was obtained by application of the chromatographic procedure already described.

(b) *Permanganate oxidation of* 2-*hydroxymethylenecholest*-4-*en*-3-*one* (IX).—Ethyl formate (0·4 g.) was added with cooling to a suspension of alcohol-free sodium methoxide (from 0·12 g. of sodium) in dry benzene (5 c.c.). A solution of cholest-4-en-3-one (10 g.; *Org. Synth.*, 1941, **21**, 18) in benzene (5 c.c.) was added to the suspension with shaking and cooling. Next day ice-water was added and the yellow precipitate collected and washed with benzene. The dried residue was shaken with a mixture of ether and dilute hydrochloric acid. The ethereal layer was separated, dried, and evaporated, leaving 2-*hydroxymethylenecholest*-4-*en*-3-*one* (1·0 g.) as a gum which crystallised readily, and separated from light petroleum (b. p. 40—60°) in pale yellow, elongated prisms, m. p. 111—112° (Found: C, 81·3; H, 10·7. $C_{28}H_{44}O_2$ requires

C, 81·6; H, 10·7%). Meanwhile the preparation of this compound has been reported by Burr, Holton, and Webb (*J. Amer. Chem. Soc.*, 1950, **72**, 4903), who give m. p. 112—113°.

The product was soluble in dilute sodium hydroxide solution but the sparingly soluble sodium salt soon separated. With ferric chloride a deep reddish-purple colour was developed. Ultraviolet absorption maxima at 250 mμ (log ε 4·1) and 310 mμ (log ε 3·8) were observed.

Powdered potassium permanganate (25 g.) was added, in small quantities during 30 minutes, to a stirred solution of hydroxymethylene cholestenone (4·8 g.) in acetone (100 c.c.), the temperature being kept at 0—5°. The precipitate was collected, dried in air, and suspended in water (150 c.c.). Sulphur dioxide was passed into the suspension, with cooling, until a clear solution was obtained. The solution was acidified and extracted with ether. Evaporation gave an acidic gum which was heated at 170—180° for 30 minutes. The decarboxylated material was taken up in ether and extracted with alkali. Evaporation of the dried etheral solution gave a neutral gum (0·4 g.), which, when subjected to chromatography as previously described, gave the Inhoffen ketone (0·2 g.), m. p. 52°.

Des-A-cholestan-5-one-6 : *6-di-ββ-propionic Acid* [*2'* : *2'-Bis-2''-carboxyethyl-1-(1* : *5-dimethylhexyl)perhydro-3'-keto-7a* : *4'-dimethyl-4* : *5-benzindene*] (XXI).—A mixture of the Inhoffen ketone (1·11 g.), dioxan (5 c.c.), "Triton B" (1 c.c.), and acrylonitrile (0·18 g.) was kept for 40 hours at the room temperature and then acidified. Evaporation of the dioxan left an oil which was boiled for 22 hours with aqueous potassium hydroxide (30 c.c. of 20%). The cooled and diluted solution was freed from neutral matter with ether, acidified, and extracted with ether. Evaporation of the ether gave a gum (0·15 g.) which slowly crystallised on trituration with acetone. The *acid* separated from a large volume of acetone in rhombs, m. p. 275—277° (decomp.) (Found: C, 72·8; H, 10·1%; equiv., 243·0. $C_{29}H_{48}O_5$ requires C, 73·1; H, 10·1%; equiv., 238).

6-Methylanilinomethylenedes-A-cholestan-5-one [*1-(1* : *5-Dimethylhexyl)perhydro-3'-keto-7a* : *4-dimethyl-3'-N-methylanilinomethylene-4* : *5-benzindene*] (XXII).—The condensation of the Inhoffen ketone (2·3 g.) with ethyl formate (1·05 g.) in ether (10 c.c.) in the presence of sodium methoxide (from 0·4 g. of sodium) under the usual conditions (see above) furnished the hydroxymethylene derivative of the ketone as a yellow oil (2·4 g.), which gave a purplish-red colour in alcoholic ferric chloride. Reaction of the hydroxymethylene-ketone (2·1 g.) with methylaniline (0·75 g.) in benzene (10 c.c.), by the procedure described above in another example, afforded *6-methylanilinomethylenedes-A-cholestan-5-one* (2·4 g.) which separated from light petroleum (b. p. 40—60°) as cream-coloured needles, m. p. 116—117° (Found: C, 83·1; H, 10·2. $C_{31}H_{47}ON$ requires C, 82·9; H, 10·5%).

Des-A-cholestan-5-one-10-β-propionic Acid (*Windaus Acid*) (VII).—A mixture of the above methylanilinomethylene-ketone (6·6 g.), dioxan (90 c.c.), "Triton B" (7·5 c.c.), and acrylonitrile (1·0 g., 1·25 mol.) was kept at the room temperature for 48 hours. The mixture was acidified and the dioxan evaporated. The oily residue was boiled for 30 minutes with hydrochloric acid (120 c.c. of 10%), and the oil which separated taken up in ether, and the ether evaporated. The residual oil was heated under reflux with potassium hydroxide (150 c.c. of 20%) for 20 hours. The cooled and diluted solution was freed from neutral matter with ether and acidified. The acid solution was extracted four times with ether; evaporation left an acidic gum (0·7 g.), which was taken up in a little ether and kept at 0° for several days, a crystalline mass then forming slowly. The crystals were collected (0·6 g.), m. p. 143—144°, and recrystallised from ether–light petroleum (b. p. 40—60°). The product was so obtained in glistening needles, m. p. 154°, alone or mixed with a specimen made by oxidation of cholestenone (Windaus, *loc. cit.*). Mrs. D. M. Hodgkin kindly carried out *X*-ray diffraction determinations on the synthetic and the authentic material, and reported that the two specimens were identical.

Evaporation of the mother-liquors gave an acidic gum (0·1 g.) from which no further crystalline matter could be obtained. This gum probably contained some of the epimeric form of the Windaus acid.

Des-A-cholest-6-en-5-one [*1-(1* : *5-Dimethylhexyl)-Δ²'-decahydro-3'-keto-7a* : *4'-dimethyl-4* : *5-benzindene*] (XXV).—A solution of Inhoffen's ketone (1·0 g.) in acetic acid (40 c.c.) was cooled and shaken during the dropwise addition of a solution of bromine (1·0 g.) in acetic acid (10 c.c.). The mixture was poured into ice-water, and the oily product isolated with ether. The ethereal solution was washed with aqueous sodium hydrogen carbonate until neutral, then dried, and the solvent evaporated. A dark-red, fuming syrup remained (1·5 g.). The same product was eventually obtained when half the quantity (1 mol.) of bromine was employed. The crude bromo-ketone (XXV) (1·5 g.) in collidine (10 c.c.) was heated under reflux at 185° for 1 hour. The cooled mixture was freed from collidine hydro-

bromide by filtration (yield, 0·75 g.) and the residue washed thoroughly with ether. The filtrate was concentrated, finally *in vacuo*, the dark oily product taken up in ether, and the ethereal solution washed with dilute acid. Evaporation of the dried ethereal solution gave a brown gum which distilled at 180—190° (bath)/0·0005 mm. (0·4 g.), and at 175—180° (bath)/0·0003 mm. (Found: C, 83·6; H, 11·6. $C_{29}H_{48}O$ requires C, 83·6; H, 11·5%). The product showed a maximum absorption in the ultra-violet at 235 mμ (log ε 4·2). This suggests that it is *des*-A-*cholest*-6-*en*-5-*one* (XXV), the calculated $\lambda_{max.}$ for this structure according to Woodward's rule (*J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 76) being 227 mμ, and for the isomeric structure (XXVI), 254 mμ.

The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in glistening, deep-red plates, m. p. 175—176° (decomp.) (Found: C, 68·2; H, 8·4. $C_{29}H_{42}O_4N_4$ requires C, 68·2; H, 8·2%).

Grateful acknowledgment is made to the Royal Commissioners for the Exhibition of 1851 for the award of a Senior Studentship to one of us (A. R. P.). We thank Messrs. Charles Lennig and Co. Ltd., for a gift of " Triton B " and Messrs. E. I. du Pont de Nemours and Co., Inc., for a gift of 1 : 3-dichlorobut-2-ene.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, November 8th*, 1951.]

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222. *The Preparation and Properties of Selenium Tetrafluoride and Oxyfluoride.*

By E. E. AYNSLEY, R. D. PEACOCK, and P. L. ROBINSON.

A preparation of selenium oxyfluoride from the dioxide is described in which there is no accompanying formation of any oxy-compound of sexavalent selenium. At 0° with low concentrations of fluorine, selenium tetrafluoride has been obtained from the element in high yield. Some physical properties of these liquids have been measured. Selenium tetrafluoride shows remarkable solvent properties and gives selenofluorides with alkali fluorides.

SELENIUM oxyfluoride was first obtained by Prideaux and Cox (*J.*, 1927, 929; 1928, 738) by reaction of silver fluoride with selenium oxychloride, and its formation in other reactions has been noted by Wiechart (*Z. anorg. Chem.*, 1950, **261**, 313) and Huckel (*Nachr. Akad. Wiss. Göttingen*, Math.-phys. Klasse, 1946, 36—37). No recent examination of its properties has, however, been made and there is evidence that earlier preparations were not pure.

A new method of preparing selenium oxyfluoride by the action of well-diluted fluorine on selenium dioxide has proved successful. Under ideal experimental conditions, yields of oxyfluoride reaching 80% of the dioxide used are possible. The rest of the selenium appears as a gas, which on condensation and fractionation, proves to be selenium hexafluoride. A second method of preparation, producing satisfactory yields of the oxyfluoride, is the combustion of selenium in a stream of fluorine containing about 60% of oxygen. The oxyfluoride from either source, after redistillation in a vacuum, requires no further purification and does not attack dry glass. Its m. p. is 15·0°, some 10° higher than that previously reported, and its b. p. is 126°. The molecular weight of the vapour is normal. The density at 20° is 2·800 g./c.c. and the surface tension, measured by capillary rise, 42·2 dynes/cm. at 25° The parachor, calculated from the surface tension and density measurements, is abnormal [$(P)_{obs.} = 121$; $\Sigma(P) = 133{\cdot}9$]. Selenium oxychloride shows a similar abnormality [$(P)_{obs.} = 179{\cdot}1$; $\Sigma(P) = 191{\cdot}1$].

Lebeau (*Compt. rend.*, 1907, **144**, 1092, 1196, 1397; **145**, 190) got a liquid fluoride, together with the well-known gaseous selenium hexafluoride, by passing fluorine over selenium contained in a copper boat; he reported the liquid to be the tetrafluoride. Prideaux and Cox (*J.*, 1927, 928; 1928, 1608) obtained a similar material by reaction of silver fluoride with selenium tetrachloride, and determined some of its properties. Yost and Clausen (*J. Amer. Chem. Soc.*, 1933, **55**, 885), in the course of fractionating selenium hexafluoride, collected a liquid which they were unable to analyse as the vessel containing it exploded. They described this substance as an unstable lower fluoride.

We have shown that diluted fluorine reacts with selenium at 0° to give the tetrafluoride. At temperatures above 100°, or with more concentrated fluorine which raises the temperature in the zone of reaction, the main product is the gaseous hexafluoride, so it is necessary, in order to obtain a good yield of the tetrafluoride, to use a very shallow bed of selenium on a well-cooled surface. This precaution also avoids the concurrent formation of oxyfluoride by traces of oxygen in the gas stream. Minute amounts of the latter present in the tetrafluoride considerably affect its m. p.

Pure selenium tetrafluoride melts at −9·5° to a colourless liquid which boils at 106°. The molecular weight of the vapour is normal. The density of the liquid is 2·72 at 25°, and the surface tension 34·3 dynes/cm. at 25°, giving a parachor $(P)_{obs.} = 137{\cdot}2$ [$\Sigma(P) = 165{\cdot}3$]. The compound shows little resemblance to the tetrachloride, which is a solid melting under pressure at 305° ± 3° and subliming at 196°.

The fluorides of sodium, potassium, rubidium, and cæsium dissolve in selenium tetrafluoride to form complexes with a composition approaching $MSeF_5$, a formula different from that of the other complex selenium halides, *viz.*, M_2SeX_6. These substances apparently possess an appreciable vapour pressure of selenium tetrafluoride and dissociate slowly in a vacuum even at room temperature, a behaviour similar to that of potassium iodohexafluoride, KIF_6, described by Emeléus and Sharpe (*J.*, 1949, 2206). Water immediately decomposes them. Thallous fluoride also dissolves in selenium tetrafluoride to form an isolable complex of similar formula, but with silver fluoride, the complex, although evidently formed, is very unstable.

Barium and lithium fluorides retain some tetrafluoride on drying, suggesting that combination takes place. Lithium fluoride is peculiar in being soluble in cold but not in hot selenium tetrafluoride—a behaviour which is explicable if the complex is stable at the ordinary but not at higher temperatures. Ammonium fluoride dissolves somewhat in the cold, but on being warmed the solution soon becomes brown and selenium is deposited, suggesting that the ammonium salt dissociates. The results of other qualitative reactions are given in the experimental section and these, together with the quantitative evidence, suggest that selenium tetrafluoride may be an ionising solvent. This is being investigated.

Experimental

Selenium Oxyfluoride ($SeOF_2$).—The all-glass (Pyrex) apparatus used allowed for the careful vacuum-drying of the selenium dioxide, for the fractionation of the product in a vacuum, and its distribution, under these rigorous conditions, into vessels appropriate for its analysis and the measurement of its various physical properties. The dry dioxide was treated with a nitrogen stream carrying fluorine at the rate of 2 l. per hour. The crude product was condensed, and subsequently fractionated, in a vacuum, with the removal of head and tail fractions. The final product was analysed by breaking a weighed bulb containing the material under water and determining the selenium as silver selenite and the fluorine as lead chlorofluoride (Found: Se, 59·0; F, 28·6. Calc. for $SeOF_2$: Se, 59·3; F, 28·6%).

The m. p. was observed by freezing a specimen in a water-bath containing ice and allowing the temperature to rise gradually. At 15·0° it was possible to maintain an equilibrium between solid and liquid.

The b. p. was determined by means of a capillary, with its upper end closed, dipping into the liquid which was heated by means of a bath to above the actual temperature and allowed to cool until bubbles ceased to issue from the capillary (Siwoloboff's method). The average value was 126·0°.

Determinations of the relative density of the vapour made by Dumas's method at 150° (24° above the b. p.) indicated a molecular weight of 133·5 (Calc. for $SeOF_2$: 133). Hence the vapour is not associated.

The density and coefficient of expansion were measured by the thermometer-bulb method, the vessel employed having been previously calibrated as to volume by using mercury. Observations made between 21° and 60° on 1·3580 g. of the oxyfluoride were as follows, giving a coefficient of expansion of 0·00114 c.c. per c.c. per degree:

Temp. of bath	21·5°	33·0°	42·0°	59·7°
Volume, c.c.	0·4839	0·4903	0·4949	0·5044
Density, g./c.c.	2·800	2·769	2·744	2·693

The surface tension was observed by sealing some of the liquid in a tube containing two capillaries of different, but uniform, diameters which had been previously calibrated for capillary rise by using water. As the oxyfluoride wets glass only with difficulty, special precautions were taken to flood the capillaries by tilting the whole unit immediately before making the cathetometer readings. But in spite of all precautions, reproducible results were difficult to secure : $\gamma(25^\circ) = 42$ dynes/cm., giving a parachor of 121 (Calc. : 134).

The oxyfluoride is violently hydrolysed by water, attacks phosphorus with inflammation, and gives coloured solids with potassium chloride, bromide, and iodide. Sulphur and selenium dissolve to give, respectively, a brown and a green solution, but there is little dissolution of tellurium.

Selenium Tetrafluoride.—Selenium, spread as a shallow layer on the flat base of a large reaction vessel, was dried at 200° in a vacuum and in part sublimed on to the walls, and was then treated with a 1 : 1 fluorine–nitrogen mixture at the rate of 1 l. per hour, the reaction vessel being cooled in ice. At the completion of the reaction the liquid product, which in the main remained in the reaction vessel, was distilled forward and fractionated in a vacuum. It was analysed exactly as for the oxyfluoride (Found : Se, 51·0; F, 48·2. Calc. for SeF_4 : Se, 51·0; F, 49·0%).

1. *Physical properties.* The m. p. and b. p. were observed by the methods used for the oxyfluoride, and the b. p. also by measuring the temperature at the head of a fractionating column while the liquid was being distilled in an atmosphere of dry nitrogen. The m. p. appeared to be much affected by the presence of traces of impurity; m. p. −9·5°, b. p. 106°. A determination of the molecular weight by Dumas's method gave 154 (Calc. for SeF_4 : 155).

The density was found by the method used for the oxyfluoride. Observations made between 12° and 40° with 1·4063 g. of the tetrafluoride were as follows, giving a coefficient of expansion of 0·00092 c.c. per c.c. per degree :

Temp. of bath	12·3°	18·0°	27·9°	32·5°	38·7°
Volume, c.c.	0·5085	0·5114	0·5159	0·5181	0·5210
Density, g./c.c.	2·765	2·750	2·725	2·714	2·699

The surface tension measured by capillary rise averaged 34·3 dynes per cm., which gave a parachor of 137 against a calculated value, assuming four covalencies, of 165.

2. *Reactions with metallic fluorides.* The metallic fluorides were dissolved in the selenium tetrafluoride and the compounds formed were allowed to crystallise from excess of the solvent. In some cases, however, most of the liquid tetrafluoride present had to be removed (in a vacuum at room temperature) before crystallisation could take place.

(*a*) Lithium fluoride was soluble in the cold (0·05 g. in 10 g. of solvent), but on warming, a flocculent precipitate appeared which redissolved as the solution cooled. Only a trace of selenium tetrafluoride remained associated with the solid on evaporation of the liquid.

(*b*) Sodium fluoride (0·02 g.) dissolved slowly in boiling selenium tetrafluoride (6 g.). White crystals of the double *fluoride* slowly separated on cooling, which after removal of excess of solvent at 25° were creamy-white and dissolved in water with decomposition and evolution of heat (Found : Se, 38·9; F, 48·0; Na, 13·1%; $NaF : SeF_4 = 1·18 : 1$. $NaSeF_5$ requires Se, 40·1; F, 48·2; Na, 11·7%).

(*c*) Up to 0·15 g. of potassium fluoride dissolved readily in 10 g. of tetrafluoride on warming. On cooling the solution, a precipitate slowly separated which was recrystallised by redissolving it in a smaller quantity of solvent and cooling it slowly. The crystals of the double *fluoride* were isolated by removing excess of solvent in a vacuum at 25° (Found : Se, 35·4; F, 44·5; K, 18·9%; $KF : SeF_4 = 1·05 : 1$. $KSeF_5$ requires Se, 37·1; F, 44·6; K, 18·3%).

(*d*) Rubidium fluoride (0·1 g.) dissolved in 10 g. of tetrafluoride in the cold, and, after some of the solvent had been removed, as with potassium fluoride, the complex *fluoride* crystallised (Found : Se, 28·7; F, 36·3; Rb, 34·1% $RbF : SeF_4 = 1·18 : 1$. $RbSeF_5$ requires Se, 30·4; F, 36·6; Rb, 33·0%).

(*e*) Cæsium fluoride was readily soluble in the cold (0·3 g. in 10 g. of solvent) and most of the solvent had to be removed before crystallisation started. The double *salt* formed in this case was more stable than the others and showed only slight decomposition after 24 hours in a high vacuum at room temperature (Found : Se, 24·9; F, 30·7; Cs, 43·6%; $CsF : SeF_4 = 1·01 : 1$. $CsSeF_5$ requires Se, 25·7; F, 30·9; Cs, 43·4%).

(*f*) Thallous fluoride proved to be as soluble as potassium fluoride. After the solution had cooled and excess of solvent had been removed, a well-crystallised white solid remained which had a slight vapour pressure of selenium tetrafluoride (Found : $TlF : SeF_4$, 1·03—1·15 : 1; Tl, 57·2—58·5 ; Se, 18·8—20·7. $TlSeF_5$ requires Tl, 54·0; Se, 20·9%).

(*g*) Barium fluoride gave a residue with a ratio $BaF_2 : SeF_4$ 1·40 : 1, suggesting that a compound is formed which is not very stable.

(*h*) Silver fluoride dissolved on warming (0·05 g. in 10 g. of solvent) and gave a white precipitate on cooling the solution. As the solvent was removed, however, it began to decompose: an examination at an intermediate stage suggested the formula $AgSeF_5$. After 1 hour at 100° in a vacuum the material was visibly decomposed and the ratio $AgF : SeF_4$ was as low as 1 : 0·26. The best intermediate analysis gave the ratio $AgF : SeF_2 = 1·3 : 1$.

(*i*) Calcium fluoride, practically insoluble, retained only a trace of tetrafluoride after excess had been removed.

3. *Other observations.* Selenium tetrafluoride is decomposed violently by water and attacks phosphorus as does the oxyfluoride. It is miscible in all proportions with sulphuric acid, alcohol, ether, and iodine pentafluoride, and dissolves appreciable quantities of carbon tetrachloride, chloroform, bromine, iodine, sulphur, and selenium. Selenium tetrafluoride dissolves and reacts with all the potassium halides and some of the higher metallic and non-metallic oxides such as phosphoric oxide, vanadium pentoxide, and chromium trioxide. These reactions are in the course of quantitative investigation.

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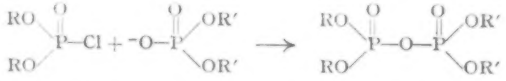
223. *Studies on Phosphorylation. Part X.* The Preparation of Tetraesters of Pyrophosphoric Acid from Diesters of Phosphoric Acid by Means of Exchange Reactions.*

By N. S. CORBY, G. W. KENNER, and A. R. TODD.

The mechanism of the reaction between tetraphenyl pyrophosphate and dibenzyl hydrogen phosphate in presence of bases (Mason and Todd, *J.*, 1951, 2267) has been elucidated and the reaction has been extended to the preparation of other symmetrical and unsymmetrical pyrophosphates. The scope of this exchange reaction has also been extended to include the preparation of pyrophosphates by treating salts of diesters of phosphoric acid with arylsulphonyl halides and with trifluoroacetic anhydride.

ONE of the principal aims of current work in these laboratories is the synthesis of dinucleotide coenzymes (*e.g.*, cozymase, flavin-adenine-dinucleotide). The mononucleotides have been synthesised through intermediates in which the hydroxyl groups of phosphoric acids were blocked by benzyl groups (Baddiley and Todd, *J.*, 1947, 648; Baddiley, Michelson, and Todd, *J.*, 1949, 582; Michelson and Todd, *J.*, 1949, 2476, 2487; Brown and Todd, *J.*, 1952, 44). If the route to dinucleotide coenzymes is to be analogous, it will involve the preparation of unsymmetrical tetra-esters of pyrophosphoric acid from which two protecting benzyl groups will be removed in a later stage of the synthesis. The object of the present investigation has been to study on simple substances the preparation of tetraesters of pyrophosphoric acid by methods which might be applicable in the nucleotide field.

Hitherto unsymmetrical tetraesters of pyrophosphoric acid have always been prepared by reaction of a chlorophosphonate with the salt of a phosphate:



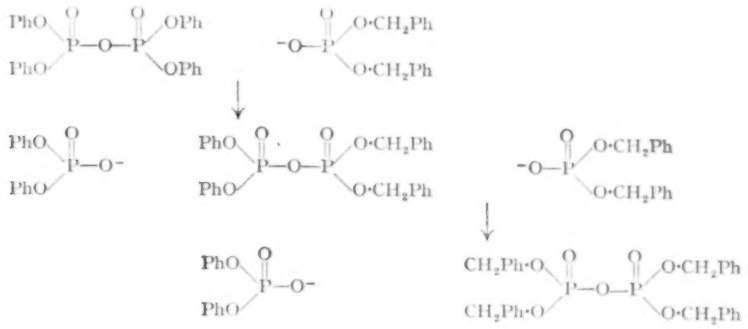
Thus the tribenzyl ester of adenosine-5′ pyrophosphate (ADP) has been prepared from dibenzyl chlorophosphonate and silver adenosine-5′ benzyl phosphate (Baddiley and Todd,

* Part IX, *J.*, 1951, 2271.

loc. cit.). Toy (*J. Amer. Chem. Soc.*, 1950, **72**, 2065) has described the preparation of some simple unsymmetrical tetraesters by the analogous reaction of pyridinium salts and chlorophosphonates in ethereal solution. Now, whereas compounds such as adenosine-5′ benzyl phosphate and their salts are now relatively freely available, the corresponding chlorophosphonates are difficultly accessible for reasons already discussed in Part VIII of this series (Mason and Todd, *J.*, 1951, 2267). Recently we have indeed been able to prepare them, and will report upon them later, but the present work was devoted to consideration of alternative routes to pyrophosphates which do not entail the use of chlorophosphonates.

In Part VIII (*loc. cit.*) the direct conversion of simple diesters of phosphoric acid into their anhydrides by reaction with thionyl chloride and oxalyl chloride was reported; these reagents, proved quite unsatisfactory for work in the nucleotide field. The striking observation was, however, made (*loc. cit.*) that tetrabenzyl pyrophosphate could be prepared in high yield from dibenzyl hydrogen phosphate by reaction for a short time with tetraphenyl pyrophosphate at room temperature in anhydrous polar solvents in presence of a tertiary base. These conditions are well-nigh ideal for work with nucleotides and it was therefore important to examine more closely the nature and scope of the process. It was of particular interest to study the possibility of halting the reaction at an intermediate stage so as to obtain an unsymmetrical pyrophosphate.

The first point which we sought to establish about the nature of the conversion of dibenzyl hydrogen phosphate into tetrabenzyl pyrophosphate by means of tetraphenyl pyrophosphate was the function of the tertiary base. Accordingly the proportion of triethylamine added was varied in a series of experiments with one mol. of tetraphenyl pyrophosphate and two of dibenzyl hydrogen phosphate in acetonitrile solution. No tetrabenzyl pyrophosphate was isolated from reaction mixtures to which one mol. or less of triethylamine had been added. An 80% yield of pyrophosphate resulted when two mols. of base were used, but this fell with increasing quantities, being only 54% when the amount of base was increased to four mols. The obvious conclusion was that the base was required to form a salt of dibenzyl hydrogen phosphate. In confirmation two mols. of lithium dibenzyl phosphate were found equally effective as two of the free acid with two of triethylamine. These findings are in accord with the mechanism of a two-stage nucleophilic displacement, already mentioned in Part VIII (*loc. cit.*) and now set out in full below :



Two mols. of base are necessary to form the two mols. of dibenzylphosphate anion. It follows from this reaction scheme that the experiment conducted with only a single mol. of triethylamine should have led to the intermediate dibenzyl diphenyl pyrophosphate as well as triethylammonium diphenyl phosphate and dibenzyl hydrogen phosphate. The isolation of this unsymmetrical pyrophosphate as such from the reaction mixture would obviously be difficult, and therefore its independent preparation was investigated in order to facilitate its detection in the mixture.

As already mentioned, unsymmetrical pyrophosphates may be prepared by the interaction of silver dialkyl phosphates and chlorophosphonates. Indeed some years ago Dr. H. T. Howard (Thesis, Cambridge, 1946) prepared crude dibenzyl diphenyl pyrophosphate

from diphenyl chlorophosphonate and silver dibenzyl phosphate in acetonitrile solution. However the alternative procedure of Toy (*loc. cit.*) using pyridinium salts in benzene solution appeared cleaner and in fact was known to be preferable to the silver salt method (Mason and Todd, *loc. cit.*) for the preparation of tetraphenyl pyrophosphate (see Experimental section). When benzene solutions of pyridinium dibenzyl phosphate and diphenyl chlorophosphonate were mixed, precipitation of pyridine hydrochloride soon started. After three hours this was removed by filtration and the filtrate evaporated at a low temperature. An opalescent gum remained, which was insoluble in water but slowly hydrolysed during six hours in contact with water maintained at pH 8 by addition of dilute ammonia, producing only a little tetrabenzyl pyrophosphate. Addition of *cyclo*hexylamine to a benzene solution of the gum precipitated *cyclo*hexylammonium diphenyl phosphate; evaporation of the solution gave dibenzyl *cyclo*hexylaminophosphonate in an amount corresponding to 90% of the dibenzyl hydrogen phosphate used in its preparation. Clearly the mode of preparation and properties of this gum leave no doubt that it is almost entirely the desired mixed anhydride, dibenzyl diphenyl pyrophosphate. Its final purification by molecular distillation could not be achieved owing to the pyrolytic decomposition characteristic of benzyl esters of phosphorus oxy-acids. On the other hand, di-*p*-methoxyphenyl diphenyl pyrophosphate, prepared analogously from diphenyl chlorophosphonate and pyridinium di-*p*-methoxyphenyl phosphate, could be successfully distilled. During the distillation, however, it evidently disproportionated into tetraphenyl pyrophosphate and tetra-*p*-methoxyphenyl pyrophosphate, for on treatment with aniline it gave mixtures of anilinium salts and mixtures of anilinophosphonates. In contrast, the oil before distillation yielded only di-*p*-methoxyphenyl aminophosphonate on dissolution in liquid ammonia. The unsymmetrical tetraesters of pyrophosphoric acid should therefore be regarded as very susceptible to disproportionation and Toy's claims (*loc. cit.*) that they can be distilled should be regarded with reserve in the absence of further experimental data.

The preparation and knowledge of the properties of dibenzyl diphenyl pyrophosphate enabled us to get further insight into the reaction between dibenzyl hydrogen phosphate and tetraphenyl pyrophosphate. The reaction between two mols. of the former, one of the latter, and one of triethylamine led to an oil moderately stable to water. Addition of *cyclo*hexylamine to a benzene solution of the product of reaction between equimolar amounts of the three reagents in acetonitrile caused precipitation of 80% of the diphenyl phosphoric residues as *cyclo*hexylammonium diphenyl phosphate. From the liquors dibenzyl *cyclo*hexylaminophosphonate was obtained in amount corresponding to 72% of the dibenzyl hydrogen phosphate used. A similar reaction in dimethylformamide, with *cyclo*hexylamine substituted for triethylamine, gave an 81% yield of dibenzyl *cyclo*hexylaminophosphonate. Moreover, tetrabenzyl pyrophosphate was produced on addition of equimolar amounts of triethylamine and dibenzyl hydrogen phosphate to the unsymmetrical pyrophosphate prepared by Toy's method. In our view the mechanism written above for the reaction in which the anhydride condition is exchanged between diesters of phosphoric acid is fully substantiated. It remains to consider the factors controlling the direction of this "exchange reaction."

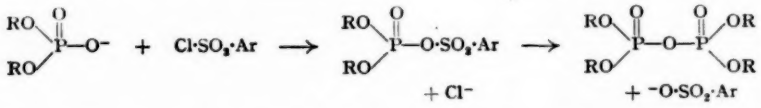
One characteristic of the "exchange reaction" is clear from the preceding account of a single case. Through it an anhydride of a diester of phosphoric acid (*i.e.*, a tetraester of pyrophosphoric acid) is converted into a less reactive anhydride. Thus tetraphenyl pyrophosphate must be stored in sealed containers to prevent its hydrolysis by atmospheric moisture, whereas tetrabenzyl pyrophosphate may be prepared by the reaction between dibenzyl phosphite, carbon tetrachloride, and aqueous alkali (Atherton and Todd, *J.*, 1947, 674) and it was isolated throughout the work described in this paper by solidification under aqueous ammonia at pH 8. The intermediate dibenzyl diphenyl pyrophosphate is correspondingly intermediate in its resistance to hydrolysis. A second point also emerges from the results presented above. The diphenyl phosphate anion must be considerably more stable in acetonitrile solution than the dibenzyl phosphate anion, otherwise the equilibrium between the two anions would permit the "exchange reaction" to proceed in presence of only catalytic quantities of base. In other words, diphenyl hydrogen phosphate must be a stronger acid than dibenzyl hydrogen phosphate and in consequence the anhydrides

derived from them have corresponding relative reactivities. To test the validity of these conclusions we determined by electrometric titration the p*K*'s of diphenyl and dibenzyl hydrogen phosphates in 50% aqueous ethanol. The values so obtained (1·84 and 1·87 respectively) differ by scarcely more than the experimental error. In non-aqueous solvents the acids would be expected to be much weaker and the differences to be more pronounced. The exact determination of acid dissociation constants in non-aqueous media is difficult, but in closely related series of compounds the strengths of acids are closely related to the conductivities of their solutions (cf. Verhoek, *J. Amer. Chem. Soc.*, 1936, **58**, 2577). Accordingly we measured the electrical resistance of decimolar solutions of diphenyl and dibenzyl hydrogen phosphate in acetonitrile and dimethylformamide. The resistance of the cell was lowered from 265 000 ohms with pure acetonitrile to 30 000 ohms by the first compound and to 87 000 ohms by the second, and from 309 000 ohms with pure dimethylformamide to 4400 and 22 200 ohms respectively. In these solvents (*i.e.*, those in which the " exchange reaction " is normally carried out), therefore, diphenyl hydrogen phosphate is a considerably stronger acid than dibenzyl hydrogen phosphate: its anion is, therefore, correspondingly more stable and its anhydride less stable. Further, decimolar solutions of di-*p*- and di-*o*-methoxyphenyl hydrogen phosphates in dimethylformamide had resistances of 5800 and 12 700 ohms respectively: their triethylammonium salts " exchanged " with tetraphenyl but not with tetrabenzyl pyrophosphate. Di-*p*-nitrophenyl hydrogen phosphate, on the other hand, gave a resistance in dimethylformamide under the same conditions of 700 ohms and had a p*K* of 1·72 in 50% aqueous ethanol. No evidence of its triethylammonium salt " exchanging " with tetraphenyl pyrophosphate could be found. The anhydride derived from this acid should be a powerful reagent and, partly with the intention of completing the series of examples of the " exchange reaction," we attempted to prepare it. Di-*p*-nitrophenyl hydrogen phosphate dissolved slowly in a boiling chloroform solution of thionyl chloride and evaporation of the solvent left a yellow solid. Although this gave, with *cyclo*hexylamine, *cyclo*hexylammonium di-*p*-nitrophenyl phosphate and di-*p*-nitrophenyl *cyclo*hexylaminophosphonate, it was not tetra-*p*-nitrophenyl pyrophosphate. It contained sulphur, liberated sulphur dioxide on hydrolysis, and underwent no " exchange reaction " with triethylammonium diphenyl phosphate: it is presumably analogous in structure to the compound produced from dibenzyl hydrogen phosphate and oxalyl chloride (Mason and Todd, *loc. cit.*). Nor could the pyrophosphate be prepared from the reaction mixture of *p*-nitrophenol, phosphoryl chloride, and pyridine, although this did give di-*p*-nitrophenyl *cyclo*hexylaminophosphonate with *cyclo*hexylamine and di-*p*-nitrophenyl hydrogen phosphate on alkaline hydrolysis.

The elucidation of the nature of this " exchange reaction " between diesters of phosphoric acid and tetraesters of pyrophosphoric acid enabled us to reinterpret the results of some earlier work. This had been directed towards the preparation of mixed anhydrides of toluene-*p*-sulphonic acid and phosphoric acids, such as dibenzyl toluene-*p*-sulphonyl phosphate. Preliminary studies with silver salts in heterogeneous media were unsatisfactory and we turned to the reaction between lithium dibenzyl and diphenyl phosphates and toluene-*p*-sulphonyl chloride in dimethylformamide solution. It was possible to follow the progress of reaction very conveniently by the decrease in electrical resistance of the solution with time as lithium chloride was eliminated. In some twenty minutes the resistance had reached a constant value but this was never as low as would be expected for complete reaction. Moreover, after addition of ammonia to the reaction mixture, the appropriate aminophosphonate, phosphoric acid, and toluene-*p*-sulphonamide were all isolated. Initially we had thought that this mixture of products had arisen from cleavage of the mixed anhydride in two directions. The same products would, however, arise if the mixed anhydride reacted rapidly with more lithium salt to give a pyrophosphate and thus half the toluene-*p*-sulphonyl chloride remained unchanged. This explanation accords better with the magnitude of the drop in electrical resistance of the solution. Since the arysulphonic acids are much stronger acids than the diesters of phosphoric acid, the intermediate anhydride would be expected to be much more susceptible to " exchange reactions."

In confirmation of these views tetrabenzyl pyrophosphate could be isolated after reaction between triethylammonium dibenzyl phosphate and toluene-*p*-sulphonyl chloride in aceto-

nitrile. The more reactive *p*-nitrobenzenesulphonyl chloride was found to be a preferable reagent however, and gave an 80% yield of tetrabenzyl pyrophosphate. This reagent was also evidently able to form the anhydrides of di-*o*-methoxyphenyl hydrogen phosphate and even di-*p*-nitrophenyl hydrogen phosphate, for the corresponding *cyclo*hexylaminophosphonates were obtained after treatment of the reaction products with *cyclo*hexylamine.



The expansion of the scope of the " exchange " type of reaction to include the formation of anhydrides of diesters of phosphoric acid by means of arylsulphonyl chlorides promoted the search for alternative reagents. Trifluoroacetic anhydride appeared to be attractive. It has been used in the esterification of carboxylic acids, and mixed anhydrides have been postulated as intermediates in the reaction (Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976). It was indeed found to be an effective reagent for the preparation of tetrabenzyl and tetraphenyl pyrophosphates, although, unlike *p*-nitrobenzenesulphonyl chloride, it did not react with triethylammonium di-*p*-nitrophenyl phosphate. The milder character of trifluoroacetic anhydride was shown in another way. Whereas the intermediate dibenzyl *p*-nitrobenzenesulphonyl phosphate could not be detected in the reaction mixtures of dibenzyl pyridinium phosphate and the sulphonyl chloride, the corresponding process with trifluoroacetic anhydride appeared to lead to dibenzyl trifluoroacetyl phosphate; for on addition of *cyclo*hexylamine no *cyclo*hexylaminophosphonate could be obtained, and if this same type of reaction was carried out in presence of one mol. of diphenyl phosphate anion addition of *cyclo*hexylamine gave an 80% yield of *cyclo*hexylaminophosphonate, *i.e.*, dibenzyl diphenyl pyrophosphate had presumably been formed from the intermediate dibenzyl trifluoroacetyl phosphate. Rather surprisingly the dimethylformamide–sulphur trioxide complex (cf. Kenner, *Chem. and Ind.*, 1951, 14) proved quite inert in reaction with lithium diphenyl and dibenzyl phosphates in dimethylformamide.

If the monobenzyl esters of mononucleotides are comparable in acid strength to dibenzyl hydrogen phosphate, this work with simple model substances has reached the original aim of the investigation, the discovery of a possible route to the dibenzyl esters of the dinucleotide coenzymes avoiding intermediate chlorophosphonates. Symmetrical tetraesters of pyrophosphoric acid can be prepared in high yield from diesters of phosphoric acid by means of *p*-nitrobenzenesulphonyl chloride. The use of the milder reagents, trifluoroacetic anhydride and tetraphenyl pyrophosphate, affords in addition the possibility of preparing unsymmetrical tetraesters. It has not been possible to isolate such unsymmetrical tetraesters in these model experiments since all the pyrophosphates studied have rather similar properties and the reactions cannot be expected to be free of by-products. It may be easier to demonstrate the formation of unsymmetrical tetraesters in the more complex nucleotide field. In considering the application of these results to nucleotide synthesis one practical point must be borne in mind. In our experience dimethylformamide, the preferred solvent for the nucleotides of high molecular weight, is by no means so satisfactory a solvent as acetonitrile. Pyrophosphates and similar compounds seem to react in some way with dimethylformamide and yields are consequently reduced.

Experimental

Tetraphenyl Pyrophosphate.—To a solution of diphenyl hydrogen phosphate (2·07 g.) in dry benzene (40 c.c.) diphenyl chlorophosphonate (1·72 c.c.) was added, followed by pyridine (0·67 c.c.). The reaction mixture was stirred magnetically at room temperature during 6 hours, moisture being rigidly excluded. Precipitated pyridine hydrochloride (0·87 g., 91%) was removed by rapid filtration through sintered glass, and benzene was removed from the filtrate by " freeze drying." The residual yellowish oil was distilled in a short-path still at 3×10^{-4} mm. Tetraphenyl pyrophosphate distilled at 150—155° as a colourless viscous oil (3·58 g., 90%), n_D^{20} 1·5610 (Found: C, 59·7; H, 4·3. Calc. for $C_{24}H_{20}O_7P_2$: C, 59·8; H, 4·2%).

Dibenzyl Diphenyl Pyrophosphate.—Dibenzyl hydrogen phosphate (0·287 g., 1 mol.) was dissolved in dry benzene (10 c.c.) and pyridine (0·08 c.c., 1 mol.) was added. This solution was slowly added to a stirred solution of diphenyl chlorophosphonate (0·22 c.c., 1 mol.) in dry benzene (5 c.c.). Pyridine hydrochloride began to separate after a few minutes and after 3 hours' stirring at room temperature the mixture was filtered and solvent removed by " freeze drying." The crude dibenzyl diphenyl pyrophosphate so obtained was a slightly opalescent viscous resin; on attempted distillation it decomposed and polymerised at *ca.* 165°. That this material consisted essentially of the mixed pyrophosphate was shown by the following experiments. Excess of *cyclo*hexylamine was added to a solution of the material in benzene. A crystalline precipitate rapidly formed and after 3 hours the mixture was filtered. The residue, which was water-soluble, appeared to be *cyclo*hexylammonium diphenyl phosphate. The filtrate was washed with dilute hydrochloric acid and water, dried (Na_2SO_4), and evaporated. Recrystallised from hexane the residue gave dibenzyl *cyclo*hexylaminophosphonate, m. p. 78—80° undepressed on admixture with an authentic specimen; the yield was 90% calculated on the assumption that the starting material was dibenzyl diphenyl pyrophosphate.

That the crude mixed pyrophosphate contained only a small amount of tetrabenzyl pyrophosphate was shown by keeping it in contact with aqueous ammonia at pH 8 for 6 hours (the pH being maintained by addition of more ammonia at intervals). Of the possible pyrophosphates present only tetrabenzyl pyrophosphate is stable under these conditions. The residue from 0·85 g. of material treated in this way was only 0·15 g. of impure tetrabenzyl pyrophosphate (m. p. 51—58°).

Di-p-methoxyphenyl Hydrogen Phosphate.—Pyridine (7·3 c.c.) was added slowly to a stirred solution of *p*-methoxyphenol (7·5 g.) and freshly distilled phosphoryl chloride (2·8 c.c.) in dry benzene (40 c.c.); heat was evolved and pyridine hydrochloride began to separate almost at once. The mixture was stirred at room temperature for 10 hours, then filtered, and the filtrate was evaporated. The yellow oily residue was dissolved in chloroform (40 c.c.) and extracted with 5% aqueous sodium hydroxide (5 × 20 c.c.). The alkaline layer was separated and acidified and the precipitated acid was extracted with chloroform (6 × 20 c.c.). The chloroform extracts were combined, dried (Na_2SO_4), and evaporated. The light brown residue was recrystallised from chloroform–light petroleum, yielding colourless needles of *di-p-methoxyphenyl hydrogen phosphate*, m. p. 92—94° (3·8 g., 41%) (Found: C, 54·0; H, 4·8. $C_{14}H_{15}O_6P$ requires C, 54·2; H, 4·85%).

Di-p-methoxyphenyl Diphenyl Pyrophosphate.—Di-*p*-methoxyphenyl hydrogen phosphate (2·21 g., 1 mol.) was dissolved in dry benzene (50 c.c.), and diphenyl chlorophosphonate (1·48 c.c., 1 mol.) was added, followed by pyridine (0·58 c.c., 1 mol.). The mixture was stirred for 8 hours at room temperature in absence of moisture, pyridine hydrochloride (91% of theory) filtered off, and the solvent removed by "freeze drying." Crude di-*p*-methoxyphenyl diphenyl pyrophosphate remained as a viscous oil (4·24 g.).

A portion (2·2 g.) of the product was treated with liquid ammonia, whereupon it became yellow and solidified. Excess of ammonia was allowed to evaporate and the residue was washed with water, giving a solid water-insoluble residue (0·84 g.). Recrystallisation from chloroform gave di-*p*-methoxyphenyl aminophosphonate, m. p. 181—183° undepressed by an authentic specimen (see below) (69%, calculated on mixed pyrophosphate).

Distillation of the crude pyrophosphate in a short-path still began at 150°/10^{-4} mm. and the main bulk of product distilled at 150—165° as a colourless oil. When treated with aniline, this gave a mixture of anilinophosphonates (m. p. 95—115°), together with a mixture of anilinium diphenyl and di-*p*-methoxyphenyl phosphates. Quantitative separation of the components was difficult but they appeared to be present in approximately equal proportions. Evidently extensive dismutation to tetraphenyl and tetra-*p*-methoxyphenyl pyrophosphates had occurred on distillation.

Di-o-methoxyphenyl Hydrogen Phosphate.—Prepared as described by Auger and Dupuis (*Compt. rend.*, 1908, **146**, 1152), the acid had m. p. 95—96° (Found: C, 53·9; H, 5·0. Calc. for $C_{14}H_{15}O_6P$: C, 54·2; H, 4·85%). Its cyclo*hexylamine* salt crystallised from ethanol in colourless needles, m. p. 161—162° (Found: C, 58·8; H, 6·7; N, 3·4. $C_{20}H_{28}O_6NP$ requires C, 58·7; H, 6·9; N, 3·4%).

Di-p-nitrophenyl Hydrogen Phosphate.—*p*-Nitrophenol (12·9 g., 2 mols.) and phosphoryl chloride (4·2 c.c., 1 mol.) were dissolved in a mixture of acetonitrile (15 c.c.) and dry benzene (120 c.c.). Pyridine (11·5 c.c., 3 mols.) was then added gradually to the cooled and stirred solution during 20 minutes. Stirring was continued at room temperature for 5 hours, then the white precipitate was filtered off, the filtrate evaporated, and the residue dissolved in chloroform.

Aqueous sodium hydroxide (40 c.c. of 5%) was added, the mixture shaken vigorously, and the yellow precipitate of sodium di-*p*-nitrophenyl phosphate was collected. The crude salt was dissolved in warm water (*ca.* 100 c.c.) and filtered from a small amount of tri-*p*-nitrophenyl phosphate (14%; m. p. 157—159° after recrystallisation from acetic acid). The filtrate was made acid to Congo-red, and the pale yellow precipitate of di-*p*-nitrophenyl hydrogen phosphate was recrystallised from ethyl acetate (yield, 7·8 g., 50%; m. p. 176—178°) (Hoeflake, *Rec. Trav. chim.*, 1916, **36**, 58, gives m. p. 175°).

Di-p-*nitrophenyl* cyclo*Hexylaminophosphonate.*—In the above preparation of di-*p*-nitrophenyl hydrogen phosphate there was some evidence that a considerable amount of the corresponding chlorophosphonate was produced. To confirm this, a separate experiment was carried out starting with 3·7 g. of *p*-nitrophenol in which the chloroform solution of the reaction product was treated with *cyclo*hexylamine (4·9 c.c.), the mixture being externally cooled. After 1 hour the mixture was washed thoroughly with hydrochloric acid, water, and aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. Recrystallisation of the yellow residue (3·1 g.) first from chloroform–light petroleum and then from benzene gave *di*-p-*nitrophenyl* cyclo*hexylaminophosphonate* as yellow needles, m. p. 174—176° (Found: C, 51·2; H, 4·9; N, 10·2. $C_{18}H_{20}O_4N_3P$ requires C, 51·3; H, 4·75; N, 10·0%).

Action of Thionyl Chloride on Di-p-nitrophenyl Hydrogen Phosphate.—Thionyl chloride (5 c.c.) was added to a suspension of di-*p*-nitrophenyl hydrogen phosphate (0·758 g., dried over phosphoric oxide at 0·1 mm.) in chloroform (25 c.c.), and the mixture was heated under reflux for 19 hours. The clear solution was evaporated to dryness under reduced pressure, yielding a yellow solid which liberated sulphur dioxide on exposure to moisture. This solid was suspended in dry chloroform (20 c.c.), and *cyclo*hexylamine (0·54 c.c.) was added, practically everything dissolving. During 6 hours at room temperature *cyclo*hexylammonium di-*p*-nitrophenyl phosphate (0·29 g.) separated as pale yellow needles; these were filtered off and the filtrate was washed first with hydrochloric acid, then with aqueous sodium hydrogen carbonate, dried, and evaporated. The residue (0·37 g.), recrystallised from benzene, gave di-*p*-nitrophenyl *cyclo*hexylaminophosphonate, m. p. and mixed m. p. 174—176°. A portion of the yellow solid product from another experiment was treated with *cyclo*hexylammonium diphenyl phosphate in the hope of effecting an exchange. No reaction appeared to take place, since treatment of the reaction mixture with *cyclo*hexylamine yielded only di-*p*-nitrophenyl *cyclo*hexylaminophosphonate.

From its general behaviour it seems possible that the yellow solid obtained in these experiments consists mainly of the mixed anhydride $(NO_2{\cdot}C_6H_4{\cdot}O)_2P(O){\cdot}O{\cdot}SO{\cdot}O{\cdot}P(O){\cdot}(O{\cdot}C_6H_4{\cdot}NO_2)_2$.

Exchange Reactions of Pyrophosphates.—(1) *Effect of amount of added base and variation of solvent.* In this group of experiments the reaction studied was that between tetraphenyl pyrophosphate and dibenzyl hydrogen phosphate to give tetrabenzyl pyrophosphate which is comparatively stable in aqueous media and can readily be isolated. In experiment (*a*) the general procedure adopted for estimating the tetrabenzyl pyrophosphate obtained is indicated; unless otherwise stated it was followed in all other examples.

(*a*) Dibenzyl hydrogen phosphate (0·724 g., 2 mols.) was dissolved in dry acetonitrile (4 c.c.), and triethylamine (0·35 c.c., 2 mols.) added. The solution was now added to tetraphenyl pyrophosphate (0·618 g., 1 mol.) in acetonitrile (1 c.c.), and the whole shaken thoroughly. After 1 hour at room temperature the solvent was removed under reduced pressure. Dilute aqueous ammonia was then added to the oily residue until pH 8 was reached. When scratched with a glass rod the oil solidified and after 30 minutes it was collected (0·545 g., 79%; m. p. 58—60°). After one recrystallisation from ether–*cyclo*hexane the product had m. p. 59—61°, undepressed on admixture with authentic tetrabenzyl pyrophosphate. For further confirmation a portion of the product was dissolved in dimethylformamide, and excess of aqueous ammonia (*d* 0·880) was added. On dilution with water colourless needles of dibenzyl aminophosphonate (m. p. and mixed m. p. 102°) separated.

(*b*) Tetraphenyl pyrophosphate (0·48 g., 1 mol.), dibenzyl hydrogen phosphate (0·557 g., 2 mols.), and triethylamine (0·42 c.c., 3 mols.) reacted under the same conditions to give tetrabenzyl pyrophosphate (0·372 g., 70%).

(*c*) Reaction as in (*b*), but using 4 mols. of triethylamine, gave 54% of tetrabenzyl pyrophosphate.

(*d*) As above but using only 0·1 mol. of triethylamine. No tetrabenzyl pyrophosphate could be isolated. The reaction product became acid (pH *ca.* 2) on addition of water and only a trace of oil (*ca.* 5 mg.) was obtained insoluble at pH 8; this may have been dibenzyl diphenyl pyrophosphate [see (*f*) below].

(*e*) As above, but in absence of any base. No reaction occurred since all the products dissolved in water giving a strongly acid solution.

(*f*) As above using 1 mol. of triethylamine. In this case no tetrabenzyl pyrophosphate was isolated but, instead, an oil was obtained which did not solidify in contact with aqueous ammonia at pH 8 in 6 hours. This oil was mainly dibenzyl diphenyl pyrophosphate as was shown by the following method. After the reactants had been mixed and set aside for 45 minutes the solvent was evaporated and benzene was added to the oily residue, followed by *cyclo*hexylamine (2 mols.). After 2 hours the crystalline precipitate of *cyclo*hexylammonium diphenyl phosphate (80%; m. p. and mixed m. p. 198—199°) was filtered off and the filtrate was washed with dilute hydrochloric acid and water, dried, and evaporated. The solid residue recrystallised from hexane gave dibenzyl *cyclo*hexylaminophosphonate, m. p. and mixed m. p. 78—80°. The yield was 72%, calculated on the assumption that the reaction product was dibenzyl diphenyl pyrophosphate; in another experiment using *cyclo*hexylamine (1 mol.) in place of triethylamine (1 mol.), and dimethylformamide in place of acetonitrile, the yield rose to 81%.

(*g*) As above using 2 mols. of triethylamine but with benzene as solvent. The yield of tetrabenzyl pyrophosphate was 64%.

(*h*) Dry lithium dibenzyl phosphate (0·690 g., 2 mols.) was dissolved in dimethylformamide (8 c.c.), and tetraphenyl pyrophosphate (0·587 g., 1 mol.) in dimethylformamide (2 c.c.) was added to the slightly turbid solution. The turbidity disappeared in 10 minutes, and after a further 50 minutes at room temperature the mixture was worked up in the usual way giving tetrabenzyl pyrophosphate (0·461 g., 71%).

(2) *Effect of acid strength.* The general method employed is set out in experiment (*a*) and, except where otherwise stated, proportions of reactants and conditions were similar throughout, the products being identified by reaction with ammonia to give aminophosphonates.

(*a*) Tetraphenyl pyrophosphate (0·64 g., 1 mol.) was added to dibenzyl triethylammonium phosphate [0·649 g. (2 mols.) of dibenzyl hydrogen phosphate + 0·2 c.c. (2 mols.) of triethylamine] in anhydrous dimethylformamide (2 c.c.) at room temperature. After 5—10 minutes aqueous ammonia (10 c.c.; *d* 0·880) was added, and the mixture shaken vigorously, set aside for 1 hour, and diluted with water to *ca.* 25 c.c. The precipitated dibenzyl aminophosphonate (0·175 g., 50% calculated on tetrabenzyl pyrophosphate) was recrystallised from carbon tetrachloride and had m. p. and mixed m. p. 102—103°.

(*b*) Tetraphenyl pyrophosphate (1 mol.) and di-*o*-methoxyphenyl triethylammonium phosphate (2 mols.), treated in the same way, gave *di-o-methoxyphenyl aminophosphonate*, crystallising from chloroform in colourless needles (90%), m. p. 68—70° (Found: C, 54·6; H, 5·4; N, 4·6. $C_{14}H_{16}O_5NP$ requires C, 54·4; H, 5·2; N, 4·5%).

(*c*) Tetraphenyl pyrophosphate reacted in the same way with di-*p*-methoxyphenyl triethylammonium phosphate, and the mixture treated with ammonia as before, gave *di-p-methoxyphenyl aminophosphonate* (58%), needles, m. p. 179—181° (from chloroform) (Found: C, 54·2; H, 5·1; N, 4·7. $C_{14}H_{16}O_5NP$ requires C, 54·4; H, 5·2; N, 4·5%).

(*d*) Tetraphenyl pyrophosphate did not appear to react with di-*p*-nitrophenyl triethylammonium phosphate under these conditions, since subsequent treatment with ammonia yielded only diphenyl aminophosphonate (48%; m. p. and mixed m. p. 147—148°).

Relative Acid Strengths of Some Diesters of Phosphoric Acid in Various Solvents.—Measurements of p*K*'s for several diesters used in this work were made in aqueous and aqueous-ethanolic solution by electrometric titration (cf. Kumler and Eiler, *J. Amer. Chem. Soc.*, 1943, **65**, 2355).

Since the majority of exchange reactions were carried out in dimethylformamide or acetonitrile or in a mixture of both, the conductivity of solutions of the various diesters of phosphoric acid in these solvents at 25° was determined.

The dimethylformamide used was purified by first storing it over solid potassium hydroxide for 24 hours, then distilling it azeotropically with benzene, and finally fractionating it under reduced pressure. It had b. p. 50—52°/15—16 mm., n_D^{19} 1·4302.

Acetonitrile was dried for 24 hours over anhydrous potassium carbonate, then refluxed with a little phosphoric oxide, decanted, and distilled from a fresh small quantity of the same desiccant. It had b. p. 82°/760 mm.

Diphenyl hydrogen phosphate which normally crystallised as the dihydrate was dried by heating the molten acid for 12 hours at 80°/0·1 mm. over phosphoric acid and then recrystallising the anhydrous product from dry chloroform–light petroleum; it then had m. p. 68—70° and was kept in a dry atmosphere.

*Reaction between Lithium Diphenyl Phosphate and Toluene-*p*-sulphonyl Chloride.*—An approximate measure of the rate of reaction between equivalent quantities of these compounds in

dimethylformamide was obtained by following the change in resistance of the mixture with time, using the circuit described by Woolf (*Chem. and Ind.*, 1950, 544). The resistance of the various reaction components was first determined in dimethylformamide with the following results (all concentrations 0·04 molar; temp. of cell, 20°).

	Resistance (ohms)		Resistance (ohms)
Pure dimethylformamide (solvent) ...	76 500	Lithium toluene-*p*-sulphonate	90
Lithium dibenzyl phosphate	922	Lithium chloride	72
Toluene-*p*-sulphonyl chloride	196		

After mixing of the reactants the resistance decreased rapidly and acquired a constant value (81·5 ohms) after 20 minutes. A similar rate was observed for the reaction between lithium di-*p*-nitrophenyl phosphate and diphenyl chlorophosphonate, but it required about 100 minutes to reach a constant resistance in the reaction between lithium diphenyl phosphate and 2 : 4 : 6-tribromobenzoyl chloride.

A solution of lithium diphenyl phosphate (2·56 g., 1 mol.) in anhydrous dimethylformamide (40 c.c.) was added to toluene-*p*-sulphonyl chloride (1·9 g., 1 mol.) in the same solvent (10 c.c.). After 2 hours at room temperature, gaseous ammonia was passed through the solution till saturated, and the mixture left for 3 hours, then evaporated under reduced pressure. The residue was extracted with chloroform (2 × 25 c.c.) and the combined chloroform extracts were filtered and extracted, first with saturated aqueous sodium hydrogen carbonate (extract A), then with 4% aqueous sodium hydroxide (extract B). The chloroform layer, dried and evaporated, gave a residue (1·41 g.) which, when recrystallised from chloroform, had m. p. 150—151° alone or mixed with authentic diphenyl aminophosphonate (yield, 46% calculated on the basis of mixed anhydride formation, or 92% calculated on tetraphenyl pyrophosphate formation).

Extract A was acidified and extracted with chloroform. The chloroform layer, dried and evaporated, gave diphenyl hydrogen phosphate (1·32 g., 46%). Extract B was acidified and evaporated to dryness, and the residue extracted with absolute ethanol (75 c.c.). When evaporated, the ethanolic extract gave toluene-*p*-sulphonamide (0·191 g., 20%), m. p. 133—134° undepressed by an authentic specimen.

*Tetrabenzyl Pyrophosphate from Toluene-*p*-sulphonyl Chloride and Salts of Dibenzyl Hydrogen Phosphate.*—To a solution of dibenzyl hydrogen phosphate (0·56 g., 1 mol.) in dry benzene (20 c.c.), toluene-*p*-sulphonyl chloride (0·382 g., 1 mol.) was added, followed by dry pyridine (0·16 c.c., 1 mol.). The mixture was stirred at room temperature for 1½ hours, whereupon it became turbid. After a further 3½ hours it was filtered and the solvent removed by "freeze drying," giving a semi-solid residue (0·952 g.). This residue was dissolved in acetonitrile (5 c.c.), and the solution filtered and evaporated. The oily residue was then treated with dilute aqueous ammonia to pH 8 in the usual manner, and yielded tetrabenzyl pyrophosphate (28%), m. p. and mixed m. p. 59—61°.

In a second experiment using triethylamine in place of pyridine, and with acetonitrile as solvent instead of benzene, the yield of isolated tetrabenzyl pyrophosphate was 47%.

Preparation of Pyrophosphates using p-*Nitrobenzenesulphonyl Chloride.*—(1) *Tetrabenzyl pyrophosphate.* Dibenzyl hydrogen phosphate (0·291 g., 1 mol.), *p*-nitrobenzenesulphonyl chloride (0·221 g., 1 mol.), and pyridine (0·08 c.c., 1 mol.) were brought into reaction in benzene as in the previous experiment. After filtration the benzene solution was divided into two portions A and B. To portion A excess of *cyclo*hexylamine (0·12 c.c.) was added, and, after 4 hours at room temperature, the solution was filtered, washed with dilute hydrochloric acid, dried, and evaporated. The residue was dissolved in warm chloroform, and light petroleum added till crystallisation set in. The product (0·04 g.) had m. p. 133—135° undepressed on admixture with authentic N-cyclo*hexyl*-p-*nitrobenzenesulphonamide*, m. p. 135—137° (Found: C, 50·8; H, 5·9; N, 10·0. $C_{12}H_{16}O_4N_2S$ requires C, 50·8; H, 5·64; N, 9·9%). The mother-liquors from the crystallisation of this product were evaporated. Recrystallised from hexane, the residue yielded dibenzyl *cyclo*hexylaminophosphonate (0·066 g., 70% calculated on the formation of tetrabenzyl pyrophosphate), m. p. and mixed m. p. 79—81°.

Portion B was "freeze dried" and the residue treated with dilute aqueous ammonia to pH 8, yielding tetrabenzyl pyrophosphate (0·095 g., 70%), isolated in the usual way.

In a second experiment, dibenzyl hydrogen phosphate (0·575 g., 2 mols.) and triethylamine (0·28 c.c., 2 mols.) were dissolved in acetonitrile (5 c.c.). The mixture was set aside at room temperature for 1 hour, then evaporated and worked up with dilute ammonia in the usual way,

giving tetrabenzyl pyrophosphate (0·431 g., 80%), m. p. 58—60°. The use of dimethylformamide as solvent in this reaction gave only a 47% yield of tetrabenzyl pyrophosphate.

(2) *Tetra-p-nitrophenyl pyrophosphate.* Di-*p*-nitrophenyl triethylammonium phosphate (2 mols.), treated with *p*-nitrobenzenesulphonyl chloride (1 mol.) in 1 : 1 acetonitrile–dimethylformamide in the same manner, gave an oil shown to be essentially the pyrophosphate by treatment with *cyclo*hexylamine (4 mols.) at room temperature; the products were di-*p*-nitrophenyl *cyclo*hexylaminophosphonate (46%; m. p. and mixed m. p. 174—176°) and *cyclo*hexylammonium di-*p*-nitrophenyl phosphate (46%).

(3) *Tetra-o-methoxyphenyl pyrophosphate.* The experiment described under (2) above was repeated, substituting di-*o*-methoxyphenyl triethylammonium phosphate for di-*p*-nitrophenyl triethylammonium phosphate. The oily product was identified as the pyrophosphate by treatment with *cyclo*hexylamine, giving *di-o-methoxyphenyl cyclohexylaminophosphonate* (80%, calculated on the assumption that the product was pyrophosphate), colourless needles (from hexane), m. p. 92—94° (Found: C, 60·9; H, 6·5; N, 3·6. $C_{20}H_{28}O_6NP$ requires C, 61·4; H, 6·65; N, 3·6%).

Preparation of Pyrophosphates by Use of Trifluoroacetic Anhydride.—(1) *Tetrabenzyl pyrophosphate.* Dibenzyl hydrogen phosphate (0·286 g., 2 mols.) was dissolved in acetonitrile (5 c.c.) and triethylamine (0·14 c.c., 2 mols.) added, followed by trifluoroacetic anhydride (0·07 c.c., 1 mol.; Stacey *et al.*, *J.*, 1949, 2976). The mixture was set aside for 1 hour at room temperature and worked up in the usual way at pH 8, giving tetrabenzyl pyrophosphate, m. p. 60—61° (0·2 g., 75%).

(2) *Tetraphenyl pyrophosphate.* The above experiment was repeated using diphenyl hydrogen phosphate in place of dibenzyl hydrogen phosphate. Owing to the instability and difficulty of isolating the tetraphenyl pyrophosphate, the product was assayed by treatment with *cyclo*hexylamine: it gave diphenyl *cyclo*hexylaminophosphonate (64%) and *cyclo*hexylammonium diphenyl phosphate (63%).

(3) *Attempted preparation of tetra-p-nitrophenyl pyrophosphate.* Di-*p*-nitrophenyl phosphate (0·49 g., 2 mols.) was dissolved in a mixture of dimethylformamide (3 c.c.) and acetonitrile (7 c.c.), and triethylamine (0·2 c.c., 2 mols.) added, followed by trifluoroacetic anhydride (0·11 c.c, 1 mol.). After 50 minutes the solvent was removed under reduced pressure, the residue taken up in dry chloroform (15 c.c.), and *cyclo*hexylamine (0·35 c.c., 4 mols.) added. The only product isolated was *cyclo*hexylammonium di-*p*-nitrophenyl phosphate, m. p. and mixed m. p. 188—190°; the recovery was 83%.

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224. *The Synthesis of Laminaribiose (3-β-D-Glucosyl D-Glucose) and Proof of its Identity with Laminaribiose isolated from Laminarin.*

By P. BÄCHLI and (the late) E. G. V. PERCIVAL.

Laminaribiose has been synthesised by the interaction of 1 : 2-5 : 6-di*iso*propylidene glucose and tetra-acetyl glucosyl bromide, proof of its formulation as 3-β-D-glucosyl D-glucose being thus obtained. The synthetic material is identical with laminaribiose prepared from laminarin. Various derivatives of the sugar are described including the α- and the β-octa-acetate, hepta-acetyl laminaribiosyl bromide, hepta-acetyl methyl-β-laminaribioside, and methyl-β-laminaribioside.

LAMINARIBIOSE was first studied by Barry (*Sci. Proc. Roy. Dublin Soc.*, 1941, **22**, 423), who isolated it as the osazone from the mixture of sugars produced by the action of the juice of *Helix Pomatia* on the polysaccharide laminarin. The free sugar, m. p. 161—162°, was obtained by the partial hydrolysis of laminarin with mineral acid. After removal of the glucose by fermentation and of the oligosaccharides by precipitation with alcohol, the disaccharide was obtained as an amorphous powder which crystallised when its aqueous solution was slowly evaporated. Earlier work by the same author (*ibid.*, 1939, **22**, 50) had shown that laminarin was composed of glucose residues mutually linked through the

1 : 3-positions by β-linkages. Since the disaccharide was hydrolysed by emulsin giving rise only to glucose, Barry formulated it as 3-β-D-glucosyl D-glucose. Laminaribiose was further studied by Connell, Hirst, and Percival (*J.*, 1950, 3494), and its identity has now been confirmed by synthesis as the result of the condensation of 2 : 3 : 4 : 6-tetra-acetyl glucosyl bromide with 1 : 2-5 : 6-di*iso*propylidene glucose.

Gakhokidze (*J. Gen. Chem. U.S.S.R.*, 1946, **16**, 1923) had previously claimed the synthesis of the α-linked analogue of laminaribiose by the condensation of 2 : 3 : 4 : 6-tetra-acetyl glucose with 4 : 6-benzylidene 1 : 2-*iso*propylidene glucose followed by alkaline and acid hydrolysis. The formulation of this as 3-α-D-glucosyl D-glucose was established by the same author in a later paper (*ibid.*, 1949, **19**, 2100). Preliminary experiments revealed that reactions of this type are by no means easy to carry out and the presence of an effective internal desiccant has been found to be essential. Helferich, Bohn, and Winkler (*Ber.*, 1930, **63**, 989) used calcium chloride in their synthesis of gentiobiose by the interaction of tetra-acetyl glucosyl bromide and 1 : 2 : 3 : 4-tetra-acetyl glucose, and Reynolds and Evans (*J. Amer. Chem. Soc.*, 1938, **60**, 2559) found the proprietary material "Drierite" enabled gentiobiose octa-acetate to be obtained in 75—80% yield. Haskin, Hann, and Hudson (*ibid.*, 1941, **63**, 1724) have also used "Drierite" in similar reactions.

In the present work 3-β-D-glucosyl D-glucose was synthesised by the condensation of tetra-acetyl glucosyl bromide with 1 : 2-5 : 6-di*iso*propylidene glucose in benzene solution in the presence of silver carbonate, iodine, and "Drierite." Deacetylation, followed by removal of the *iso*propylidene group, and separation of the products on a cellulose column gave in 9·5% yield the crystalline α-form, laminaribiose, m. p. 198—201°, $[\alpha]_D^{16}$ 25° ⟶ +18·6° in water (compare Connell, Hirst, and Percival, *loc. cit.*).

For comparison with the synthetic material, laminaribiose was prepared from laminarin. After partial hydrolysis of the polysaccharide, laminaribiose was separated from the other products on a charcoal–"Filter Cel" column of the type described by Whistler and Durso (*J. Amer. Chem. Soc.*, 1950, **72**, 677). The crystalline product had m. p. 199—202°, and gave no depression of m. p. on admixture with the synthetic material. The two samples gave identical osazones and octa-acetyl derivatives, and their *X*-ray powder photographs were indistinguishable. The formulation of natural laminaribiose as 3-β-D-glucosyl D-glucose is, therefore, definitely established. In the course of these experiments crystalline hepta-acetyl methyl-β-laminaribioside and methyl-β-laminaribioside were prepared.

After this work had been completed a synthesis of 3-β-glucosyl glucose was reported by Freudenberg and Oertzen (*Annalen*, 1951, **574**, 37), who used the same starting materials for the synthesis and obtained the crystalline β-form, m. p. 188—192°, $[\alpha]_D$ +7° ⟶ 20·8° in water, of laminaribiose, but were not in a position to compare directly the natural and the synthetic disaccharide. There is, moreover, little overlap between their work and ours since their experimental methods and the derivatives they describe are not the same as those recorded in the present paper.

Experimental

1 : 2-5 : 6-*Di*iso*propylidene* 3-(β-*Tetra-acetyl* D-*Glucosyl*) D-*Glucose*.—Pure 1 : 2-5 : 6-di*iso*propylidene glucose (10 g.), silver carbonate (15 g.), and "Drierite" (30 g.; dehydrated at 240° during 2 hours) were shaken in dry benzene (80 c.c.) for 12 hours. Iodine (3 g.) was added followed by an equimolecular proportion of 2 : 3 : 4 : 6-tetra-acetyl glucosyl bromide (15·7 g.) in dry benzene (80 c.c.), added slowly during 1 hour with constant shaking in the dark. The shaking (with occasional release of carbon dioxide from the flask) was continued until a test sample gave no precipitate with alcoholic silver nitrate (70 hours). After filtration through "Filter Cel" the unchanged di*iso*propylidene glucose (2·8 g.) was removed by repeated extraction with water (4 × 100 c.c.). The aqueous extracts showed only di*iso*propylidene glucose when examined on a paper chromatogram. The solution was dried (Na_2SO_4), treated with a little charcoal, and filtered. Removal of the solvent gave a colourless glass (*A*) (16·8 g.).

3-β-D-*Glucosyl* D-*Glucose*.—The acetyl groups were removed by shaking a solution of (*A*) in methanol (80 c.c.) for 6 hours with 0·1N-sodium methoxide (10 c.c.) at room temperature, followed by neutralisation with aqueous oxalic acid. Removal of most of the methanol at 40°/15 mm. was followed by the removal of the *iso*propylidene groups by treatment of the

residue with oxalic acid (0·01N; 150 c.c.) at 100°. After neutralisation with barium carbonate and filtration, the remaining ions were removed by Amberlite 1R-100H and 1R-4B ion-exchange resins. Evaporation of the water left a colourless syrup (*B*) (10·3 g.) (Found: Ac, nil). Examination on the paper chromatogram with pyridine showed the presence of much glucose (R_G 1·0) and of substances with R_G values 3·1, 2·1, 0·75 (laminaribiose), 0·4, and 0·25.

A column of powdered cellulose (50 × 2·8 cm.) was prepared, washed, and tested as described by Hough, Jones, and Wadman (*J.*, 1949, 2511). The syrup (*B*) (10·2 g.) was dissolved in butanol–pyridine–water (2 : 1 : 1). The elution was started with butanol (300 c.c.) followed by butanol–water–pyridine (6 : 1 : 1). The disaccharide appeared after elution of the column by butanol (300 c.c.) and butanol–water–pyridine (6 : 1 : 1) (2130 c.c.), and was present in the next 600 c.c. Removal of the solvent gave a white glass (1·242 g.; equivalent to a yield of 9·5% of theory); this crystallised slowly when a concentrated solution in ethanol was kept at 0°, and formed needles (1·17 g.), m. p. 196—199°. Further recrystallisation gave material, m. p. 204—206°, $[\alpha]_D^{15}$ +24·9° (20 minutes), +18·6° (9 hours, constant) in water (*c*, 2·5). Estimation by hypoiodite oxidation according to the method described by Hirst, Hough, and Jones (*J.*, 1949, 928) indicated that the material was 99·5—100% pure (Found: C, 42·0; H, 6·6. Calc. for $C_{12}H_{22}O_{11}$: C, 42·1; H, 6·5%).

3-β-*Glucosyl Glucosazone*.—The disaccharide (0·075 g.) on suitable treatment gave laminaribiosazone, which recrystallised from hot water containing some pyridine as long needles, m. p. 199—201°, $[\alpha]_D^{15}$ −76·0° in ethanol (*c*, 0·5) {Connell, Hirst, and Percival (*loc. cit.*) recorded $[\alpha]_D$ −71·5° for natural laminaribiosazone; Barry and Dillon (*Proc. Roy. Irish Acad.*, 1941, **22**, 423) gave −79·6°, and Freudenberg and Oertzen, −71°} (Found: C, 54·2; H, 6·4; N, 10·4. Calc. for $C_{24}H_{32}O_9N_4$: C, 55·4; H, 6·2; N, 10·7%). The osazone acetate was prepared by Muir and Percival's method (*J.*, 1940, 1480); it formed a yellow amorphous solid.

Laminarin (20 g.) was hydrolysed by heating it with aqueous oxalic acid (750 c.c.; 0·1N) at 100° for 7 hours. After neutralisation with calcium carbonate and filtration, the solution was evaporated at 40°/15 mm. to 100 c.c. Examination of the product on a paper chromatogram [solvent: benzene–*n*-butanol–pyridine–water (1 : 5 : 3 : 3)] indicated the presence of glucose (R_G 1·0), laminaribiose (R_G 0·75), and four unknown substances having R_G 0·45 and less. The mixture was separated on a column (25 × 4 cm.) of equal parts of charcoal and "Filter Cel" (Whistler and Durso, *loc. cit.*). The charcoal and "Filter Cel" had been thoroughly mixed, and a suspension in water was poured in small quantities into the column, the lower end of which was closed with a tightly pressed layer of cotton wool. The water was allowed to drain through between the additions. The column was washed with water (1500 c.c.) before use. Water was used as the eluant and after the removal of glucose and a portion of the unknown substance having R_G 0·45 (750 c.c.), a mixture of laminaribiose (1·03 g.) and the rest of the unknown of R_G 4·5 (200 c.c.) was obtained. Laminaribiose alone was present in the next 800 c.c. and its complete removal (2·62 g.) was effected by changing the eluant to water–ethanol (10 : 0·7) (1200 c.c.). The impure fraction of laminaribiose was passed through a smaller column (12 × 4 cm.). The first fraction contained the unknown sugar, R_G 0·45, and the laminaribiose (0·37 g.) was obtained after addition of 7% of alcohol to the eluant. The total yield of laminaribiose was 2·99 g. After crystallisation it had m. p. 204—206° not depressed on admixture with synthetic laminaribiose; $[\alpha]_D^{15}$ +26·5° (15 minutes), +19·5° (40 hours, constant) in water (*c*, 2·8). Through the kindness of Dr. C. A. Beevers, *X*-ray powder photographs of the natural and the synthetic product were obtained, a copper target and 1 hour's exposure (25 mA; 50 kv) being used; the two substances gave identical photographs (Found: C, 42·1; H, 6·8. Calc. for $C_{12}H_{22}O_{11}$: C, 42·1; H, 6·5%).

Octa-acetyl β-*Laminaribiose*.—Laminaribiose (0·53 g.) (from laminarin) and anhydrous powdered sodium acetate (0·26 g.) were heated with acetic anhydride (3 c.c.) at 100°. After 20 minutes the powder had dissolved, and heating was continued for a further 20 minutes. The addition of water (15 c.c.) caused the precipitation of an oil which was separated from the supernatant liquor (*C*). This oil solidified very slowly when kept under cold water. The solid (0·31 g.; m. p. 135°) was crystallised by the addition of methanol to its solution in chloroform, followed by concentration. Crystallisation was initiated by the addition of ether, followed later by light petroleum (b. p. 40—60°). After five recrystallisations *octa-acetyl* β-*laminaribiose* was obtained as prismatic needles, m. p. 160—161°, $[\alpha]_D^{15}$ −28·8° in chloroform (*c*, 2·5) (Found: C, 49·7; H, 5·7; Ac, 50·7. $C_{28}H_{38}O_{19}$ requires C, 49·6; H, 5·6; Ac, 50·7%).

Synthetic disaccharide (0·22 g.) was treated as above and after three recrystallisations from methanol–ether gave octa-acetyl β-laminaribiose (0·08 g.), m. p. 156—158° not depressed on admixture with the material just described; $[\alpha]_D^{15}$ −25·3° in chloroform (*c*, 2·2).

Octa-acetyl α-Laminaribiose.—(a) *Laminaribiose from laminarin.* The liquor (*C*) (see previous paragraph) was neutralised (sodium hydrogen carbonate) and extracted with chloroform. On evaporation of the chloroform, crude octa-acetyl laminaribiose was obtained as a yellow oil (0·6 g.). This material was isomerised by heating it with acetic anhydride (3 c.c.) and fused zinc chloride (0·04 g.) (cf. Hudson and Johnson, *J. Amer. Chem. Soc.*, 1915, **37**, 1270). After 45 minutes the mixture was cooled and water (20 c.c.) added. On the repeated addition of water and decantation, the precipitated oil solidified. After four recrystallisations of the brown solid (0·38 g.) from chloroform–ethanol *octa-acetyl α-laminaribiose* was obtained as prismatic needles containing one molecule of ethanol of crystallisation; it had m. p. 77—78°; $[\alpha]_D^{17}$ +20° in chloroform (*c*, 3·6), calculated for the ethanol-free compound (Found: Ac, 47·5, 47·8. $C_{28}H_{38}O_{19}.C_2H_6O$ requires Ac, 47·5. $C_{28}H_{38}O_{19}$ requires Ac, 50·7%). The rotation figures for the α- and the β-octa-acetate indicate that the separation of the two isomers is not quite complete (compare Hudson and Johnson, *ibid.*, 1917, **39**, 1272).

(b) *Synthetic laminaribiose.* The sugar (0·075 g.) was acetylated by the procedure described by Kruger and Roman (*Ber.*, 1936, **69**, 1832) and Nicolas and Smith (*Nature*, 1948, **161**, 349) (yield of crude octa-acetate, 51%). Recrystallisation from ethanol gave a product having m. p. 77—79°, not depressed on admixture with the octa-acetate from natural laminaribiose described above, $[\alpha]_D^{16}$ +21° in chloroform (*c*, 1·8) (Found: C, 50·0; H, 6·3; Ac, 47·9. Calc. for $C_{28}H_{38}O_{19}.C_2H_6O$: C, 49·7; H, 6·1; Ac, 47·5%). Attempts to remove the ethanol from the crystals only led to its replacement by other solvents; for instance recrystallisation from methanol gave a *product* having $[\alpha]_D^{18}$ +21·5° in chloroform (*c*, 2·56), m. p. indefinite, containing one molecular proportion of methanol of crystallisation (Found: C 49·0; H, 6·2; Ac, 48·9. $C_{28}H_{38}O_{19}.CH_4O$ requires C, 49·0; H, 6·0; Ac, 48·5%). Similar results were obtained with benzene.

Hepta-acetyl Laminaribiosyl Bromide.—Laminaribiose octa-acetate (0·6 g.; a mixture of the α- and the β-form) was added with shaking to glacial acetic acid (2 c.c.) saturated with hydrogen bromide at 0° (Latham, May, and Mosettig, *J. Org. Chem.*, 1950, **15**, 884). After 5 minutes, cooling was discontinued but shaking was continued until all the octa-acetate had dissolved (10 minutes). The viscous oil which separated was kept at 15° for 3 hours. Addition of dry toluene (20 c.c.) followed by its removal at 40—50°/12 mm. gave after two such operations a pale yellow solid (0·48 g., 83%). Crystallisation of this from chloroform–ethanol gave white needles (0·44 g.), m. p. 165—167°. After four recrystallisations from chloroform–ether–light petroleum *hepta-acetyl laminaribiosyl bromide* was obtained having m. p. 180·5—181·5° $[\alpha]_D^{18}$ +85·0° in chloroform (*c*, 3·0) (Found: C, 45·15; H, 4·9; Br, 10·8. $C_{26}H_{35}O_{17}Br$ requires, C, 44·6; H, 5·0; Br, 11·4%).

Hepta-acetyl Methyl-β-laminaribioside.—Hepta-acetyl laminaribiosyl bromide (0·32 g.), dry methanol (10 c.c.), and dry benzene (10 c.c.) [dried by shaking it with "Drierite" (3 g.) for 2 hours] were shaken in the dark with dry silver carbonate (0·5 g.) and iodine (0·1 g.) until a test sample gave no precipitate with silver nitrate (20 hours) (compare Reynolds and Evans, *J. Amer. Chem. Soc.*, 1940, **62**, 66). Chloroform (50 c.c.) was added, and after filtration aided by "Filter Cel," followed by evaporation of the solvent, a red syrup was obtained which crystallised on the addition of ethanol (yield 0·255 g., 86%). Hepta-acetyl methyl-β-laminaribioside after three recrystallisations from ethanol had m. p. 164—165°, but on further heating it resolidified and melted again at 179—180°. In another experiment the substance was obtained in the first instance as needles, m. p. 183°; nevertheless on recrystallisation it showed the double melting point, 164—165° and 179—180°, and had $[\alpha]_D^{16}$ −45° in chloroform (*c*, 1·7) (Found: C, 50·0; H, 6·0; OMe, 4·3; Ac, 48·0. $C_{27}H_{38}O_{18}$ requires C, 49·8; H, 5·9; OMe, 4·8; Ac, 47·7%).

Methyl-β-laminaribioside.—Hepta-acetyl methyl-β-laminaribioside (0·408 g.) in dry methanol (10 c.c.) was boiled with sodium methoxide (1 c.c.; 0·1N) for 1 hour (Zemplen, *Ber.*, 1936, **69**, 1827). Filtration through charcoal and removal of the solvent gave a colourless syrup, which crystallised after 4 days under alcohol. Three recrystallisations from ethanol–ether gave *methyl-β-laminaribioside* as fine needles, m. p. 165—166°, $[\alpha]_D^{19}$ −28° in water (*c*, 2·5) (Found: C, 41·9; H, 7·0; OMe, 7·8. $C_{13}H_{24}O_{11}.H_2O$ requires C, 41·7; H, 6·95; OMe, 8·3%).

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KING'S BUILDINGS, UNIVERSITY OF EDINBURGH. [*Received, December 7th*, 1951.]

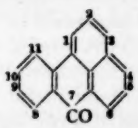
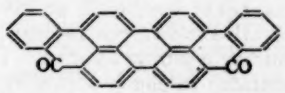
225. *The Occurrence of Direct Hydroxylation and Self-condensation in the Action of Potassium Hydroxide on Three Isomeric Benzo-derivatives of* meso*Benzanthrone.*

By WILLIAM BRADLEY and F. K. SUTCLIFFE.

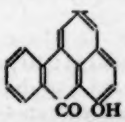
Three isomeric benzo-derivatives of *meso*benzanthrone have been prepared and their reactions with potassium hydroxide investigated. The 5 : 6-benzo-compound is characterised by the ease with which it affords a monohydroxy-derivative; at higher temperatures condensation to a derivative of violanthrone occurs. The 10 : 11-benzo-derivative undergoes self-condensation even at low temperatures, a derivative of *iso*violanthrone resulting. The 8 : 9-benzo-compound is the least reactive of the isomers; at high temperatures self-condensation to a derivative of violanthrone takes place, and a small proportion of hydroxylation occurs at the same time.

The relation between the hydroxylation and the self-condensation reactions is discussed.

*meso*BENZANTHRONE (I), heated with potassium hydroxide at 230—240°, affords a mixture of violanthrone (II) and *iso*violanthrone (III) (Bally, *Ber.*, 1905, **38**, 195; Scholl and Seer, *Annalen*, 1912, **394**, 126; Zincke, Linner, and Wolfbauer, *Ber.*, 1925, **58**, 323; Lüttringhaus and Neresheimer, *Annalen*, 1929, **473**, 259), and many simple derivatives of *meso*-benzanthrone exhibit a similar ability for self-condensation to colouring matters having the

(I)   (II)

properties of quinones. Chloro*meso*benzanthrones (G.P. 188 193, 436 533), methyl*meso*-benzanthrones (G.P. 188 193), and alkoxy*meso*benzanthrones (G.P. 413 738, 436 887, 442 511) all possess this property. The reaction depends on the presence in *meso*benzanthrone of a carbonyl group and a nucleus which readily transmits its chemical effects (Bradley and Jadhav, *J.*, 1948, 1622, 1746). 6-Hydroxy*meso*benzanthrone (IV) is stable towards fused alkalis (Bradley and Jadhav, *J.*, 1937, 1791), and this accords with the lower reactivity of the carbonyl group which results from conjugation with the hydroxyl substituent (Bradley and Sutcliffe, *J.*, 1951, 2118).

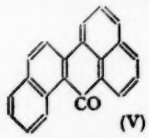
(III)  (IV)

In the present communication three ring-homologues of *meso*benzanthrone have been examined with the object of observing their ability to yield quinones of the violanthrone–*iso*violanthrone type. At the same time the compounds have been studied for their ability to undergo direct hydroxylation with alkalis as reported for *meso*benzanthrone by Perkin and Spencer (*J.*, 1922, **121**, 479) and by Bradley and Jadhav (*J.*, 1937, 1791).

The condensation of 1 : 2-benzanthraquinone with glycerol and sulphuric acid to form "benznaphthanthrone" was first described in G.P. 181 176. The constitution of the product was not then known. Scholl and Seer (*Annalen*, 1912, **394**, 111) prepared 8 : 9-benzo-*meso*benzanthrone * (V) by the ring-closure of di-1-naphthyl ketone, and Cook (*J.*, 1939, 268) showed it to be identical with "benznaphthanthrone." In the present work the condensation of 1 : 2-benzanthraquinone with glycerol yielded two products separable by crystallisation. One was the expected 8 : 9-benz*omeso*benzanthrone, the other was a

* This type of nomenclature is used for convenience in denoting the relations of isomers; Ring Index names are added in the Experimental section.

red isomeric ketone. This was considered to be 5 : 6-benzo*meso*benzanthrone (VI) for the reason that it differed from (V) and also from 10 : 11-benzo*meso*benzanthrone (VII). The 10 : 11-isomer was prepared by decarboxylating its 4'-carboxylic acid which results by partial cyclisation of 1 : 1'-dinaphthyl-8 : 8'-dicarboxylic acid (Rule and Smith, *J.*, 1937, 1096).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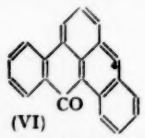
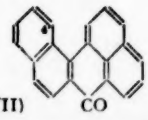

(VI)

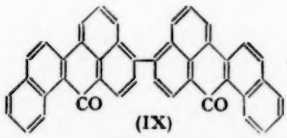

(VII)

Heating with alcoholic potassium hydroxide at 110° transforms 5 : 6-benzo*meso*-benzanthrone (VI) into a monohydroxy-derivative, an instance of unusually ready direct hydroxylation, which recalls the somewhat similar conversion of aceanthrenequinone into 1 : 9-oxalylanthr-10-one, amongst other products, by hot aqueous potassium hydroxide (Liebermann and Kardos, *Ber.*, 1914, **47**, 1203). The new product is considered to be the 4-hydroxy-derivative of (VI) since direct hydroxylation of *meso*benzanthrone yields a mixture of 4- and 6-hydroxy*meso*benzanthrones (Bradley and Jadhav, *J.*, 1937, 1791). Like 4-hydroxy*meso*benzanthrone, to which it is structurally analogous, 4-hydroxy-5 : 6-benzo*meso*benzanthrone affords a coloured and strongly fluorescent solution in aqueous alkali hydroxides.

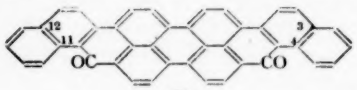
The greater ease of hydroxylation of 5 : 6-benzo*meso*benzanthrone than of *meso*benzanthrone accords with the known greater reactivity of the *meso*-ring of anthracene than of with the nucleus of naphthalene.

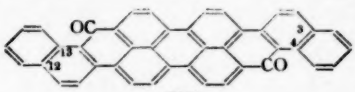
Fused with potassium hydroxide at 220—230°, 5 : 6-benzo*meso*benzanthrone yields the 4-hydroxy-derivative and a green, neutral diketone, which dissolves in alkaline dithionite (hydrosulphite) forming a purple solution. The absorption spectrum of a solution of the diketone in concentrated sulphuric acid shows the same general features as that of violanthrone in the same solvent and differs entirely from that of *iso*violanthrone. For this reason, as well as by analogy with *meso*benzanthrone, which yields violanthrone with alkalis at 220—230°, the green diketone is considered to be 6 : 7-8 : 9-dibenzoviolanthrone (VIII).

(VIII)


(IX)

The isomeric 8 : 9-benzo*meso*benzanthrone (V) behaves quite differently. There is little or no reaction at 110° with alcoholic potassium hydroxide. No hydroxylation occurs nor is there formed any di-(8 : 9-benzo*meso*benzanthron-4-yl) (IX), analogous in structure to the di*meso*benzanthron-4-yl which results easily from *meso*benzanthrone under similar conditions (Lüttringhaus and Neresheimer, *loc. cit.*). In G.P. 181 176 and 185 223 the formation of a blue diketone by the alkali fusion of " benznaphthanthrone " at 220—230° is described. 8 : 9-Benzo*meso*benzanthrone would be expected to show the same behaviour as *meso*benzanthrone, and for this reason the blue diketone should be 3 : 4-11 : 12-dibenzoviolanthrone (X). On alkali fusion of 8 : 9-benzo*meso*benzanthrone at 220° reaction

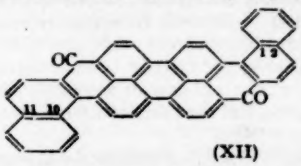

(X)


(XI)

occurred with particular ease, giving a blue colouring matter and a very small amount of a phenol which, like 4-hydroxy*meso*benzanthrone, dissolved in alkali hydroxides with a reddish-brown colour and a green fluorescence. The blue colouring matter, after purification, gave a blue solution in concentrated sulphuric acid. This showed the light absorption

characteristic of violanthrone, but there was a slight increase in the red absorption similar to that found with *iso*violanthrone but not with violanthrone, which suggested the presence of a small proportion of 3 : 4-12 : 13-dibenzo*iso*violanthrone (XI).

10 : 11-Benzo*meso*benzanthrone differs from both 5 : 6- and 8 : 9-benzo*meso*benzanthrones in its reaction with alkalis. Already at 110° it is transformed by alcoholic potassium hydroxide into a blue quinonoid diketone. A solution of the product in concentrated sulphuric acid shows a typical *iso*violanthrone absorption. For this reason it is considered to be 1 : 2-10 : 11-dibenz*iso*violanthrone (XII).

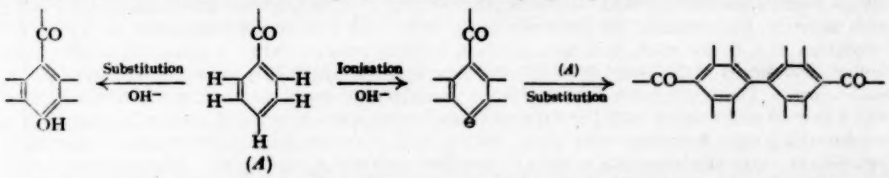


(XII)

The *trans*-union of 10 : 11-benzo*meso*benzanthrone at 110° harmonises with the known behaviour of *meso*benzanthrone, which yields violanthrone (*cis*) and *iso*violanthrone (*trans*) on alkali fusion, the proportion of *iso*violanthrone increasing the lower the reaction temperature (Lüttringhaus and Neresheimer, *loc. cit.*).

The action of alcoholic potassium hydroxide at 110° in causing the hydroxylation of 5 : 6-benzo*meso*benzanthrone and the self-coupling of 10 : 11-benzo*meso*benzanthrone affords a further illustration of the close connection between nuclear substitution by anions and the self-coupling reaction to which brief reference has already been made (Bradley and Jadhav, *J.*, 1948, 1623).

In general terms, an aromatic carbonyl compound (*A*) having the appropriate degree of nuclear reactivity may undergo either direct hydroxylation or ionisation in the presence of strong alkalis. The anion, if formed, may simulate the hydroxyl ion in forming a covalent link with carbon situated *ortho* or *para* to the carbonyl group.



(*A*)

The factors which determine the occurrence of the two reactions remain to be more fully investigated, but several points appear clear. Ketones which ionise with difficulty even in the presence of concentrated alkalis can undergo only hydroxylation. With the development of acid character the coupling reaction may occur. Finally, if the ketone is potentially a relatively strong acid, the derived anion may form a covalent link less readily and hydroxylation may become again the only important reaction. Self-condensation should occur more readily in the absence of competing hydroxyl ions. The formation of dipyridyls when pyridine is heated with sodium (Wibaut and Dingemanse, *Rec. Trav. chim.*, 1923, **42**, 240) may be a reaction of this kind, the essential intermediate being the pyridyl anion, and Brown and Hammick (*J.*, 1949, 173) have shown that the decarboxylation of quinaldic acid in quinoline yields 2 : 2'-diquinolyl, a reaction which they attribute to the intermediate formation of the 2-quinolyl anion and its subsequent union with quinoline.

Experimental

5 : 6- (VI) *and* 8 : 9-*Benzo*meso*benzanthrone* (V) (13-*Ketodibenzo*[b,mn]*phenanthrene and* 7-*Ketobenzo*[hi]*chrysene respectively*).—The crude product obtained by condensing 1 : 2-benzanthraquinone (50 g.), glycerol (50 g.), and aniline (70 g.) by the method of G.P. 181 176 was a black resin. It was extracted by means of acetone (500 c.c.). The extract was filtered hot. The orange-brown residue (18·5 g.; m. p. 137—142°), crystallised first from toluene and then from pyridine, gave two products. The less soluble 5 : 6-*benzo*meso*benzanthrone* (3·6 g.) was

obtained as long, red needles, m. p. 199·5—200·5° (Found: C, 90·0; H, 4·5. $C_{21}H_{12}O$ requires C, 90·0; H, 4·3%). The more soluble 8 : 9-benz*omeso*benzanthrone (3·25 g.) separated as short, yellow needles, m. p. 188—189° (Found: C, 89·5; H, 4·5%), and did not depress the m. p. of 8 : 9-benz*omeso*benzanthrone prepared from 1 : 1'-dinaphthyl ketone by Scholl and Seer's method (*loc. cit.*, p. 111). Whilst 8 : 9-benz*omeso*benzanthrone dissolves in concentrated sulphuric acid with a deep orange colour, 5 : 6-benz*omeso*benzanthrone affords a red solution with a slight bluish tinge. The former exhibits maxima at 5430 ($E = 2·64$) and 5820 Å ($E = 4·14$), the latter a maximum at 4950 Å ($E = 3·34$) (E = extinction coefficient for 0·002% solutions in " AnalaR " sulphuric acid contained in a cell of 2-cm. thickness).

No homogeneous material could be obtained from the acetone extract. Evaporation gave a brown solid, m. p. 120—180°, and this, repeatedly crystallised from glacial acetic acid, afforded material, m. p. 145—146°, unaltered by further crystallisation from the same solvent. A solution in benzene, passed through a column of alumina, afforded a small, dark, strongly adsorbed band containing impurities, but the main constituents formed a single, uniform, orange band.

10 : 11-*Benz*omeso*benzanthrone* (VII) (7-*Ketodibenz*[a,kl]*anthracene*).—10 : 11-*meso*Benzanthrone-4'-carboxylic acid (20 g.; m. p. 280°) (Rule and Smith, *J.*, 1937, 1096) was heated under reflux during 7 hours with quinoline (50 c.c.) and copper bronze (1 g.). The cooled suspension was filtered and the dark filtrate added to alcohol (400 c.c.). After 2 days the small precipitate was collected and the mother-liquor was added to an excess of dilute hydrochloric acid; a second precipitate formed. The combined precipitates were extracted with successive small volumes of 5% aqueous sodium carbonate (800 c.c. in all) until nothing more dissolved. The alkali extracts, united and acidified, yielded 9·5 g. of unchanged starting material, m. p. 278—280°. The alkali-insoluble material was extracted by means of glacial acetic acid. The extract was treated with charcoal, filtered, and concentrated; crystals, m. p. 178—179°, slowly separated. Recrystallisation from glacial acetic acid gave the 10 : 11-*benzo*-derivative as brownish yellow needles, m. p. 181—182° (Found: C, 89·5; H, 4·3%). The solution in concentrated sulphuric acid was brownish-red, and at lower concentrations of the solute orange-yellow.

4-*Hydroxy*-5 : 6-*benz*omeso*benzanthrone* (8-*Hydroxy*-13-*ketodibenzo*[b,mn]*phenanthrene*).—To a solution containing potassium hydroxide (10 g.) and potassium acetate (1 g.) in ethanol (20 c.c.) was added 5 : 6-benz*omeso*benzanthrone (2 g.). The mixture was heated under reflux with stirring, the internal temperature being 110°. The reactants thickened, owing to the formation of a bulky solid, and became dark reddish-brown. After 1 hour, the product was cooled, and mixed with water (200 c.c.), and the resulting suspension heated and aërated on the water-bath. The insoluble material (1·5 g.; mainly unchanged 5 : 6-benz*omeso*benzanthrone) was collected and washed with hot dilute sodium hydroxide solution and then with water. The combined alkaline solutions were pink, with a yellow fluorescence. Acidification afforded a precipitate; this was collected, washed thoroughly with water, and dried. The product (0·4 g), heated for a few minutes with boiling acetic anhydride (25 c.c.) containing a few drops of pyridine, yielded 0·4 g. of fine, pale yellow needles, m. p. 280—281° (decomp.). This derivative was insoluble in cold aqueous sodium hydroxide, but when 0·3 g. was heated with a solution of sodium hydroxide (1·5 g.) in 50% aqueous alcohol (50 c.c.) it dissolved readily to form a pink solution with a yellow fluorescence. Acidification gave 4-*hydroxy*-5 : 6-*benz*omeso*benzanthrone* (0·2 g.) as orange-yellow needles, m. p. 324—326° (decomp.), unchanged by further crystallisation from nitrobenzene (Found: C, 84·4; H, 4·2. $C_{21}H_{12}O_2$ requires C, 85·1; H, 4·1%). It dissolved in concentrated sulphuric acid with a pink colour and a yellow-green fluorescence (maximum light absorption at 5400 Å; $E = >5·0$).

6 : 7-8 : 9-*Dibenzoviolanthrone*.—5 : 6-Benz*omeso*benzanthrone (2 g.) was added to a melt of potassium hydroxide (10 g.) and potassium acetate (1 g.) at 220—230°. The mixture rapidly became greenish-black. After 1 hour it was cooled and extracted with water (200 c.c.), and the resulting suspension was heated on the steam-bath and aërated; finally it was filtered. The alkaline extract, acidified, yielded 0·2 g. of a light brown product which crystallised from nitrobenzene in needles, m. p. 318—320°, not depressed on admixture with 4-hydroxy-5 : 6-benz*omeso*benzanthrone, m. p. 324—326°. The alkali-insoluble material (1·7 g.) was stirred for 3 hours with a cold solution of sodium dithionite (4 g.) and sodium hydroxide (5 g.) in water (200 c.c.). A purple solution resulted and this was filtered from a residue of impure 5 : 6-benz*omeso*benzanthrone. The filtrate, aërated, afforded a greenish-black precipitate (1·3 g.); this was collected, washed, and dried. A portion of the product dissolved in trichlorobenzene was passed through an alumina column. The solute was strongly adsorbed but development with a large volume of trichlorobenzene afforded two adjacent bands; the more strongly

adsorbed was blue-black, the more mobile red. The bands were separated and the colouring matters eluted by means of cresol at 100°. The red band afforded a small amount of 5 : 6-benzo*meso*benzanthrone. The blue-black band afforded a solution which when concentrated and then mixed with toluene yielded 6 : 7-8 : 9-*dibenzoviolanthrone* as a greenish-black powder (Found : C, 90·5; H, 4·1. $C_{42}H_{20}O_2$ requires C, 90·7; H, 3·6%). It dissolved in concentrated sulphuric acid forming a reddish-brown solution (maximum light absorption at 5250 Å; $E = 0·98$). It afforded a purple solution in alkaline dithionite.

Action of Alkalis on 8 : 9-*Benzo*meso*benzanthrone and* 10 : 11-*Benzo*meso*benzanthrone.*— 8 : 9-Benzo*meso*benzanthrone (1·0 g.), heated under reflux with a solution of potassium hydroxide (5 g.) and potassium acetate (0·5 g.) in ethanol (10 c.c.) at 110° (inner temp.), afforded mainly unchanged material, soluble in benzene, together with 0·05 g. of a violet-black, benzene-insoluble product which dissolved with a deep blue colour in alkaline dithionite containing pyridine. There was no evidence of hydroxylation.

Stirred at 220—230° for 15 minutes, 8 : 9-benzo*meso*benzanthrone (3 g.), potassium hydroxide (15 g.), and potassium acetate (1·5 g.) afforded a dark product most of which separated from the melt. This product consisted of a small quantity of a phenol, soluble in alkalis with a reddish-brown colour and a green fluorescence, and alkali-insoluble material (3 g.). The latter, extracted with boiling 1 : 2 : 4-trichlorobenzene (100 c.c.), afforded a residue (1·5 g.). All but 0·3 g. of this dissolved in hot cresol (200 c.c.), and 0·5 g. separated on cooling. Recrystallisation from quinoline yielded bluish-black 3 : 4-11 : 12-*dibenzoviolanthrone* (?), m. p. > 360° (Found : C, 89·0, 88·8; H, 3·7, 3·9. $C_{42}H_{20}O_2$ requires C, 90·7; H, 3·6%) which dissolved in concentrated sulphuric acid with a blue colour (light absorption maximum at *ca.* 4800 Å; $E = 1·1$). It dissolved with a blue-green colour in alkaline dithionite containing pyridine.

10 : 11-Benzo*meso*benzanthrone (0·5 g.) was stirred under reflux with potassium hydroxide (2·5 g.), potassium acetate (0·25 g.), and 95% alcohol (5 c.c.) at 110° (inner temp.) for 2·5 hours. The product was added to water, and the insoluble solid (0·5 g.) collected. This was dried and extracted by boiling trichlorobenzene, and the residue was taken up in hot cresol. Addition of alcohol to the cresol solution precipitated 0·21 g. of a bluish-black 1 : 2-10 : 11-*dibenzisoviolanthrone* (?) which dissolved in concentrated sulphuric acid with a green colour [light absorption maxima at 6540 ($E = 3·1$) and 7250 Å ($E = 1·8$)], m. p. > 360° (Found : C, 87·4, 87·1; H, 4·9, 3·1. $C_{42}H_{20}O_2$ requires C, 90·7; H, 3·6%). It dissolved with a blue colour and a red fluorescence in sodium hydroxide solution containing sodium dithionite.

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226. *The Reactions of Highly Fluorinated Organic Compounds. Part I. The Preparation and Reactions of Some Chloroundecafluorocyclohexanes.*

By J. C. TATLOW and R. E. WORTHINGTON.

The fluorination of *o*-dichlorobenzene in the vapour phase with cobaltic fluoride gave mainly chloroundecafluoro*cyclo*hexane and 1 : 2-dichlorodecafluoro*cyclo*hexane. The former was obtained also by a similar fluorination of chlorobenzene. Chloroundecafluoro*cyclo*hexane, when treated with lithium aluminium hydride, gave the corresponding fluoro-hydrocarbon, undecafluoro*cyclo*hexane, by exchange of hydrogen for chlorine. This reacted with aqueous alkali, being converted by loss of hydrogen fluoride into perfluoro*cyclo*hexene. From this olefin the dibromo- and dichloro-addition products were prepared, and oxidation afforded perfluoroadipic acid which was converted into certain derivatives.

THE reaction of organic compounds in the vapour phase with certain transition-element fluorides in which the metal exerts its highest valency state is a convenient method for effecting full fluorination of organic structures. The method has been used fairly extensively for the conversion of hydrocarbons into fluorocarbons, cobaltic fluoride being the

fluorinating agent most widely employed (Fowler *et al.*, *Ind. Eng. Chem.*, 1947, **39**, 292; Benner *et al.*, *ibid.*, p. 329; Burford *et al.*, *ibid.*, p. 319; Irwin *et al.*, *ibid.*, p. 350; Haszeldine and Smith, *J.*, 1950, 3617; Barber, Burger, and Cady, *J. Amer. Chem. Soc.*, 1951, **73**, 4241; Barbour, Barlow, and Tatlow, *J. Appl. Chem.*, in the press). Other metallic fluorides used for fluorocarbon synthesis have been silver difluoride (McBee and Bechtol, *Ind. Eng. Chem.*, 1947, **39**, 380), manganese trifluoride and cerium tetrafluoride (Fowler *et al.*, *ibid.*, p. 343), and lead tetrafluoride (McBee and Robb, U.S.P. 2 533 132; *Chem. Abs.*, 1951, **45**, 2975).

Compounds containing elements in addition to carbon and hydrogen have been fluorinated by this general method; thus, vapour-phase fluorination of amines and of pyridine derivatives with cobalt trifluoride to give perfluoro-amines has been reported (Thompson and Emeléus, *J.*, 1949, 3080: Haszeldine, *J.*, 1950, 1638, 1966; *J.*, 1951, 102), and by the use of the same reagent the compound CSF_8 has been produced from methanethiol and carbon disulphide (Silvey and Cady, *J. Amer. Chem. Soc.*, 1950, **72**, 3624). All these derivatives are chemically inert and in this respect resemble the fluorocarbons. Attempts to fluorinate methyl alcohol (Kellogg and Cady, *ibid.*, 1948, **70**, 3986) and aliphatic ketones (Holub and Bigelow, *ibid.*, 1950, **72**, 4879) with cobaltic fluoride were unsuccessful.

As part of our general study of highly fluorinated organic compounds, we wished to investigate certain perfluorinated chloro-derivatives and to examine their reactions. Some results obtained a few years ago suggested that when chlorofluorocarbon mixtures were fluorinated in the vapour phase by means of cobaltic fluoride, removal of the whole of the chlorine was difficult; similar observations have been made by Couper *et al.* (*Ind. Eng. Chem.*, 1947, **39**, 346), and by McBee *et al.* (*ibid.*, p. 310). Accordingly, we decided to attempt to synthesise the desired perfluorinated chloro-compounds by treatment of chlorohydrocarbons, having the same carbon skeletons, in the vapour phase with cobalt trifluoride. This paper describes the preparation, from chlorobenzene and *o*-dichlorobenzene, of chloroundecafluoro*cyclo*hexane and 1 : 2-dichlorodecafluoro*cyclo*hexane, together with certain reactions of chloroundecafluoro*cyclo*hexane. While the work was in progress, Lindgren and McBee (U.S.P. 2 480 081; *Chem. Abs.*, 1950, **44**, 2020) described the fluorination of *o*-dichlorobenzene with silver difluoride and with manganese trifluoride to give the same two products though apparently in somewhat less pure forms than ours, and McBee, Robb, and Ligett (U.S.P. 2 493 007; *Chem. Abs.*, 1950, **44**, 5375) claimed that chlorine was retained in organic structures during fluorinations with cerium tetrafluoride.

For the fluorination of chloro-compounds we found that the apparatus and conditions of reaction which were most suitable were those already used by us for fluorocarbon production (see Barbour, Barlow, and Tatlow, *loc. cit.*). The reaction vessel which we have developed for carrying out vapour-phase fluorinations with cobaltic fluoride is a horizontal electrically-heated nickel tube in which the cobalt trifluoride (*ca.* 3500 g.) is gently stirred during the reaction. To obtain the maximum yields of fully fluorinated products careful control of the reaction conditions, particularly temperature, is necessary. When chlorobenzene was fluorinated with cobaltic fluoride, chloroundecafluoro*cyclo*hexane and perfluoro*cyclo*hexane were formed. The maximum yields (*ca.* 14%) of the former were obtained when the chloro-compound (input rate 22 g./hr.) was fluorinated at 350°, care being taken to avoid temperature increases in the reaction zone. At lower reaction temperatures, increased proportions of partly fluorinated material were found in the products; below 300°, recycling of the crude product through the fluorination apparatus was necessary, and much lower overall yields were obtained. When chlorobenzene was fluorinated at 350° at higher input rates, the temperature of the reaction zone unavoidably increased, owing to the faster reaction rate, and again low yields of chloroundecafluoro*cyclo*hexane resulted. It was found that in the fluorination of *o*-dichlorobenzene, perfluoro*cyclo*hexane and three chlorofluoro*cyclo*hexanes were produced; the best reaction conditions found were almost the same as for chlorobenzene. *o*-Dichlorobenzene gave, on fluorination, chloroundecafluoro*cyclo*hexane in rather better yields (*ca.* 16%) than those obtained from chlorobenzene, the expected 1 : 2-dichlorodecafluoro*cyclo*hexane in about equal yields, and in addition small yields (*ca.* 4%) of trichlorononafluoro*cyclo*hexane. Thus, *o*-dichlorobenzene is by far the better starting material for the synthesis of chlorofluoro*cyclo*hexanes.

As in the case of chlorobenzene, lower reaction temperatures gave rise to less completely fluorinated products.

Much of the chlorine present in the chlorobenzenes was retained in the molecules during the fluorination process, though a proportion was eliminated, perfluoro*cyclo*hexane being present in all products, and chloroundecafluoro*cyclo*hexane resulting from the fluorination of *o*-dichlorobenzene. Part of the displaced chlorine was present in the elemental form in the cooled traps in which the reaction products were collected. It is noteworthy, however, that the eliminated chlorine, either in the elementary form or as chlorine fluorides, is capable of re-entering the organic structures, as shown by the formation of trichlorononafluoro*cyclo*hexane during the fluorination of *o*-dichlorobenzene, and of dichlorodecafluoro*cyclo*hexanes during the fluorination of chlorobenzene, though in the latter case no pure compound was isolated. Careful temperature control during the fluorination, the use of low feed rates, and the utilisation of less than 50% of the " available fluorine " of the reactor were necessary in order to get maximum yields of the desired products. The avoidance of recycling stages is also advantageous, since in fluorinations of this type, though yields are calculated most conveniently from the amount of organic starting material employed, the fluorine consumption, and the number of runs which can be carried out in a cobaltic fluoride reactor in a given time, are usually the most important factors.

The chlorofluoro*cyclo*hexanes obtained are all low-melting volatile solids, which are rather more soluble in the common organic solvents than are fluorocarbons. It is interesting that many of the saturated highly-fluorinated *cyclo*hexane derivatives have melting points above room temperature, and exist as low-boiling solids. This fact makes fractional distillation and other operations difficult in certain cases.

Some of the reactions of chloroundecafluoro*cyclo*hexane and of compounds derived from it are described below. Further reactions, including those of 1 : 2-dichlorodecafluoro*cyclo*hexane and the trichlorononafluoro*cyclo*hexane which were obtained, will be reported later.

Preliminary investigations, in which the monochloro-compound was treated under drastic conditions with a number of reagents which react readily with alkyl halides, showed, as expected, that these fluoro-derivatives were very stable. Aqueous alkalis, metallic salts such as acetates, cyanides, nitrites, and iodides, and metals such as sodium and magnesium could not be induced to react except under extreme conditions of temperature and pressure in certain cases, in which complete degradation resulted. It was found, however, that reaction with lithium aluminium hydride occurred readily, much chloride ion but no fluoride ion being detected after the addition of water to the reaction mixture.

The reactions of lithium aluminium hydride with hydrocarbon-type chloro-, bromo-, and iodo-derivatives have been studied recently, and, in general, with primary and secondary aliphatic halides the halogen atom is replaced by hydrogen, the order of reactivity being iodides > bromides > chlorides (Nystrom and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3738; Johnson, Blizzard, and Carhart, *ibid.*, p. 3664; Trevoy and Brown, *ibid.*, 1949, **71**, 1675). Bromo*cyclo*hexane gives *cyclo*hexane in poor yield only, and chloro*cyclo*hexane does not react (Johnson, Blizzard, and Carhart, *loc. cit.*).

The reaction of chloroundecafluoro*cyclo*hexane with lithium aluminium hydride in ethereal solution resulted in replacement of the chlorine atom by a hydrogen atom, the fluorinated structure remaining intact and the product being undecafluoro*cyclo*hexane, a compound already reported by Fukuhara and Bigelow (*J. Amer. Chem. Soc.*, 1941, **63**, 2792) who obtained it from the vapour-phase fluorination of benzene by fluorine–nitrogen mixtures in a vessel packed with copper gauze. It is also one of the products of the vapour-phase fluorination of benzene by cobaltic fluoride at temperatures below those necessary for fluorocarbon production (Barbour, Mackenzie, Stacey, and Tatlow, unpublished work). The ready replacement of chlorine by hydrogen in the reaction of chloroundecafluoro*cyclo*hexane with lithium aluminium hydride is rather surprising, in view of the general stability of chloro-fluoro-compounds and the failure of chloro*cyclo*hexane to give a similar reaction.

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Little has been reported so far about the reactions of highly fluorinated compounds retaining a few hydrogen atoms in the molecule. We found that undecafluoro*cyclo*hexane

reacted readily with concentrated aqueous alkali to give perfluoro*cyclo*hexene by elimination of a molecule of hydrogen fluoride. This olefin was reported recently by Brice and Simons (*J. Amer. Chem. Soc.*, 1951, **73**, 4017), being a product of the decomposition of undecafluoro-*cyclo*hexanecarboxylic acid in aqueous solution.

Perfluoro*cyclo*hexene possesses an unreactive double bond and undergoes the expected addition reactions only with difficulty. For instance, it reacts with chlorine only in a sealed tube; the dichloro-addition product was identical with the material obtained from the fluorination experiments with *o*-dichlorobenzene. Brice and Simons (*loc. cit.*) obtained the same dichloro-addition product. They mention the lack of reactivity of the olefin and failed to get a dibromide. We obtained this 1 : 2-dibromodecafluoro*cyclo*hexane by reaction of bromine with the olefin whilst the mixture was irradiated with light from a mercury-vapour lamp. Further, by oxidation of the olefin with aqueous potassium permanganate, perfluoroadipic acid was obtained, and was identified as the free acid and as the dianiline salt. McBee, Wiseman, and Bachman (*Ind. Eng. Chem.*, 1947, **39**, 415) obtained crude perfluoroadipic acid by fluorination of hexachlorobenzene with antimony pentafluoride to give 1 : 2-dichloro-octafluoro*cyclo*hex-1-ene, followed by oxidation of this olefin, but they did not isolate the acid itself, only derivatives. We prepared the diethyl ester and the diamide of perfluoroadipic acid; they were identical with those described by the above authors.

Further reactions of perfluorinated chloro-, polyfluoro-, and perfluoro-olefin derivatives of the *cyclo*hexane series are now being studied. A similar series of conversions proceeding in an analogous fashion to that described above has been carried out already starting from 1 : 2-dichlorodecafluoro*cyclo*hexane. It would appear that reactions of these types offer novel routes for the synthesis of many new fluorinated compounds of known constitution. These reactions enable the convenient cobaltic fluoride fluorination method, and related processes, to be employed for the production of highly fluorinated compounds which are starting points for general synthetic chemistry, and from which a variety of derivatives, hitherto inaccessible, may be made. Previously, by the use of this type of fluorination process, only chemically inert materials have been produced. Several new perfluorinated chloro-compounds have been made already, and the further reactions of these derivatives are being examined.

Experimental

Apparatus and Procedure for Fluorinations.—(a) *Cobalt trifluoride reactor.* The fluorination unit and the cell for generation of fluorine which were used in this investigation are described by Barbour, Barlow, and Tatlow (*loc. cit.*). The cobalt trifluoride reactor was a horizontal nickel tube (3′ 6″ long; $3\frac{3}{8}$″ internal diam.) fitted with a coaxial nickel stirrer shaft carrying paddles and driven at approx. 4 revs./min. The vessel was heated by seven electrical heaters, each controlled by a Simmerstat or a variable transformer. Temperatures were measured by chromel–alumel thermocouples. One of these was enclosed in a long, thin, copper tube which could be moved along inside the stirrer shaft, which was made of stout nickel tube. Temperature readings could thus be taken inside the reactor body; other thermocouples brazed on to the reactor shell gave the temperatures of the body itself. Organic materials were fed into the apparatus from a constant-rate dropper. Liquid displaced by a piston, lowered by a synchronous electric motor, ran down a heated sloping inlet tube into the reactor. After passage over the cobaltic fluoride, the products passed up a short exit tower fitted with baffle plates and were condensed in copper vessels cooled by solid carbon dioxide–alcohol. The reactor was charged with about 3500 g. of cobalt trifluoride, the " available " fluorine being approx. 575 g.

(b) *Distillation.* Fractional distillations were carried out by using glass vacuum-jacketed columns 1′ and 2′ long. When necessary, side-heaters of the type designed by Massingham (*Chem. and Ind.*, 1951, 31) were employed. Still-heads were of the simple manually-operated type incorporating capillary taps. The most suitable column packing was found to be Dixon gauze cylinders (Dixon, *J. Soc. Chem. Ind.*, 1949, **68**, 88), size $\frac{1}{16}$″ × $\frac{1}{16}$″, made of nickel gauze (100 mesh; 42 s.w.g.). Take-off rates were usually of the order of 10 c.c./hr., and the ratios of material condensed on the total condenser to that taken off were about 20 : 1 on the rises and 10 : 1 on the flats of the distillation curves. Difficulty was experienced with the low-boiling materials which were solids at normal temperatures, and to collect such products it was necessary

to use a cooled receiver almost totally enclosed, and to warm the side-arm of the still-head by means of an electric lamp or a small heater to prevent crystallisation. Removal of perfluoro-*cyclo*hexane (which sublimes at 52—53°) from the products of fluorination experiments was best accomplished by using an unjacketed column (which could be heated quickly if necessary to avoid blockages) and a simple direct take-off with no reflux. The yields of various fractions recorded below are minimum values only, since combination of intermediate fractions from different experiments followed by re-fractionation gave further quantities of pure materials.

Fluorination of Chlorobenzene.—The general method was the same as that described for the fluorination of hydrocarbons by Barbour, Barlow, and Tatlow (*loc. cit.*). The best conditions appeared to be as follows.

Chlorobenzene (110·0 g.; input rate 22 g./hr.) was passed into the cobalt trifluoride reactor, which was kept throughout at 350°, temperature increases due to the heat of reaction being avoided by adjustment of the heater controls and removal of lagging segments if necessary. After completion of the addition, the apparatus was swept out with a stream of nitrogen, and the fluorinated product was poured into ice-water, separated, washed with water, dried (P_2O_5), and filtered. The crude products (430 g.) from two such experiments were combined and fractionated. Two pure compounds were obtained: perfluoro*cyclo*hexane, subliming at 52—53°, and chloroundecafluoro*cyclo*hexane (89·2 g., 14%) which crystallised spontaneously, b. p. 79·4—80·1°/754 mm., m. p. 30—31°, n_D^{40} 1·301 (Found: C, 22·6; Cl, 11·7; F, 65·9%; *M*, 318. Calc. for C_6ClF_{11}: C, 22·8; Cl, 11·2; F, 66·0%; *M*, 316·5). Lindgren and McBee (*loc. cit.*) gave b. p. 76·9—77·0° and m. p. 24—26° for this compound.

Other experiments gave the following results: chlorobenzene (220 g.), fluorinated in two experiments at 250° (input rate 22 g./hr.), yielded C_6ClF_{11} (55·1 g., 9%) after recycling of the product under the same conditions; chlorobenzene (220 g.), fluorinated in two experiments at 300° (input rate 22 g./hr.), yielded C_6ClF_{11} (77·7 g., 13%); and chlorobenzene (110 g.) at 350° (input rate 33 g./hr.) yielded C_6ClF_{11} (17·5 g., 6%).

Fluorination of o-*Dichlorobenzene.*—By the same general method as in the case of chlorobenzene, *o*-dichlorobenzene (139 g.; input rate 26 g./hr.) was fluorinated at 350°, care being taken to avoid temperature increases. The crude product (445 g.) from two such experiments, after being washed with water, dried (P_2O_5), and filtered, was fractionated. After removal of perfluoro*cyclo*hexane, three pure crystalline compounds were isolated: chloroundecafluoro-*cyclo*hexane (96·0 g., 16%), b. p. 79·0—79·7°/746 mm., n_D^{45} 1·297, m. p. 30—31°, identical with the specimen already mentioned; 1 : 2-dichlorodecafluoro*cyclo*hexane (98·8 g., 16%), b. p. 109·6—110·2°/756 mm., m. p. 39—41°, n_D^{45} 1·382 (Found: C, 21·7; Cl, 21·9; F, 57·6%; *M*, 334. Calc. for $C_6Cl_2F_{10}$: C, 21·6; Cl, 21·3; F, 57·1%; *M*, 333); and *trichlorononafluoro*cyclo*hexane* (27·5 g., 4%), b. p. 140·7—141·2°/758 mm., m. p. 32·5—33·5°, n_D^{45} 1·363 (Found: C, 20·4; Cl, 30·6; F, 49·6%; *M*, 348. $C_6Cl_3F_9$ requires C, 20·6; Cl, 30·45; F, 48·9%; *M*, 349·5). Lindgren and McBee (*loc. cit.*) gave b. p. 107·5—107·7°, m. p. 12—14°, and n_D^{20} 1·3413 for 1 : 2-dichlorodecafluoro*cyclo*hexane, and Brice and Simons (*loc. cit.*) recorded b. p. 108°, m. p. 18·5—20°, n_D^{20} 1·338—1·339. Lindgren and McBee (*loc. cit.*) mentioned a trichlorononafluoro*cyclo*hexane, b. p. 144—148°, obtained by treatment of hexachlorobenzene with lead tetrafluoride.

o-Dichlorobenzene (278 g.), fluorinated in two experiments at 300° (input rate 26 g./hr.), yielded C_6ClF_{11} (41·1 g., 7%), $C_6Cl_2F_{10}$ (77·2 g., 12%), and $C_6Cl_3F_9$ (17·4 g., 3%). The amount of crude product was greater than in the other experiment but the intermediate fractions distilling between the pure components comprised a much higher proportion of the material, suggesting that fluorination was incomplete.

*Undecafluoro*cyclo*hexane from Chloroundecafluoro*cyclo*hexane.*—A suspension of powdered lithium aluminium hydride (2·1 g.) in dry ether (120 c.c.) was stirred mechanically and cooled in water whilst a solution of chloroundecafluoro*cyclo*hexane (50·0 g.) in dry ether (50 c.c.) was added slowly, during 1 hour, the reaction being carried out under anhydrous conditions in a vessel fitted with a reflux condenser cooled by solid carbon dioxide above the usual water condenser. Heat was evolved and a bulky white precipitate was formed. The reaction mixture was stirred at room temperature for 1 hour further and was then refluxed for 2 hours. With great care, 50% sulphuric acid (20 c.c.) was added dropwise, the reaction mixture being cooled in ice. Initially, there was a vigorous reaction with a rapid refluxing of the ether. Water (130 c.c.) was then added and, when dissolution was complete, the ethereal layer was separated, the aqueous layer was extracted with fresh portions of ether, and the combined ethereal layers were washed with water, dried ($MgSO_4$), filtered, and fractionated through a 1′ column. After removal of ether there was obtained undecafluoro*cyclo*hexane (26·4 g., 59%), which crystallised on cooling,

b. p. 63·0—63·5°/757 mm., n_D^{50} 1·275, m. p. 46—48° (Found: C, 25·9; H, 0·4; F, 73·6%; *M*, 283. Calc. for C_6HF_{11}: C, 25·55; H, 0·35; F, 74·1%; *M*, 282). Fukuhara and Bigelow (*loc. cit.*) recorded b. p. 62° for this compound and said that it consisted of high- and low-melting isomers, m. p.s 41—43° and −16° to −14°, in a mobile equilibrium. We obtained no evidence of a low-melting isomer.

Non-reactivity of Chloroundecafluorocyclohexane.—No exchange of the chlorine atom for other radicals could be effected when chloroundecafluoro*cyclo*hexane was treated with any of the following reagents: aqueous sodium hydroxide, potassium or silver acetates in glacial acetic acid, aqueous-alcoholic sodium or cuprous cyanides, magnesium turnings in dry ether, phenylmagnesium bromide, molecular sodium, or sodium iodide in acetone. In general, the starting material was recovered unchanged, but in some cases complete degradation occurred under very drastic conditions.

Perfluorocyclohexene from Undecafluorocyclohexane.—Undecafluoro*cyclo*hexane (85·0 g.) was refluxed for 4 hours with potassium hydroxide (50·0 g.) in water (100 c.c.). The mixture was then allowed to cool, and the lower liquid layer was separated, washed with water, and dried (P_2O_5). Fractionation yielded perfluoro*cyclo*hexene (65·0 g., 82%), b. p. 52·0—53·0°/750 mm., n_D^{15} 1·296 (Found: C, 27·4; F, 72·2%; *M*, 257. Calc. for C_6F_{10}: C, 27·5; F, 72·5%; *M*, 262). Brice and Simons (*loc. cit.*) gave b. p. 51—52°/728 mm., n_D^{20} 1·292—1·293, for this compound.

1 : 2-*Dibromodecafluorocyclohexane from Perfluorocyclohexene.*—The olefin (2·60 g.) and bromine (1·63 g.) were refluxed together for 60 hours whilst exposed to the light from a mercury-vapour lamp. After being washed with sodium thiosulphate solution, the organic layer solidified, and was washed with water. After being dried (P_2O_5) and filtered whilst warm, the product was distilled from a small flask, giving 1 : 2-*dibromodecafluorocyclohexane* (1·30 g., 31%), b. p. 139·0—140·5° (a colourless liquid which crystallised), m. p. 31·0—32·5°, n_D^{45} 1·367 (Found: Br, 37·0; F, 44·9%; *M*, 420. $C_6Br_2F_{10}$ requires Br, 37·9; F, 45·0%; *M*, 422).

1 : 2-*Dichlorodecafluorocyclohexane from Perfluorocyclohexene.*—The olefin (4·51 g.) and liquid chlorine (*ca.* 1·5 c.c.) were heated for 40 hours in a sealed tube by means of a mercury-vapour lamp. The product was washed with dilute aqueous potassium hydroxide, then with water, and was dried (P_2O_5). Distillation from a small flask afforded 1 : 2-dichlorodecafluoro*cyclo*hexane (3·22 g., 56%), b. p. 108·0—109·0°/752 mm., n_D^{45} 1·331, which crystallised on cooling, m. p. 36—37° (Found: Cl, 21·2; F, 57·4. Calc. for $C_6Cl_2F_{10}$: Cl, 21·3; F, 57·1%). A mixture with the specimen mentioned previously had m. p. 38—40°.

Perfluoroadipic Acid from Perfluorocyclohexene.—The olefin (20·0 g.), potassium permanganate (100·0 g.), and water (300 c.c.) were heated at 100° for 24 hours in a rocking autoclave. The reaction mixture was filtered, and the filtrate was treated with sulphur dioxide until the excess of permanganate had been reduced, and then refiltered. The filtrate was acidified with concentrated sulphuric acid (50 c.c.) and was then extracted continuously with ether. The ethereal extracts were filtered and distilled to remove ether. After being dried for 15 minutes at 100°/16 mm., and then overnight *in vacuo* over phosphoric oxide, the residual white solid (19·5 g.) was recrystallised from benzene, giving the strongly acidic *perfluoroadipic acid* (15·4 g., 70%) as white, very hygroscopic needles, m. p. 133—134° (after being dried at 60° *in vacuo* over P_2O_5) [Found: C, 24·7; H, 0·8 (after correction for the water absorbed before the combustion); F, 52·5%; equiv., 145. $C_6H_2O_4F_8$ requires C, 24·8; H, 0·7; F, 52·4%; equiv., 145]. Owing to the ready hydration of this acid, pure specimens have low m. p.s after only short exposure to the atmosphere, and drying of the m. p. tubes containing the samples is advisable.

With aniline in ethereal solution perfluoroadipic acid gave the *dianilinium* salt, m. p. 212° (after recrystallisation from acetone–chloroform) [Found: C, 45·4; H, 3·6; F, 32·0%; equiv. (by titration with NaOH), 235. $C_{18}H_{16}O_4N_2F_8$ requires C, 45·4; H, 3·4; F, 31·9%; equiv., 238].

The Diamide of Perfluoroadipic Acid.—The acid (10·0 g.) was refluxed for 24 hours with ethyl alcohol (50 c.c.) and concentrated sulphuric acid (0·1 c.c.). After removal of excess of alcohol by distillation, the residue was distilled under diminished pressure to give diethyl perfluoroadipate (8·5 g., 71%), b. p. 110—111°/16 mm., n_D^{20} 1·3546 (Found: C, 33·9; H, 3·0; F, 44·3. Calc. for $C_{10}H_{10}O_4F_8$: C, 34·7; H, 2·9; F, 43·9%).

The diester (2·00 g.) was dissolved in anhydrous ether (20·0 c.c.) and ammonia was passed through the cooled solution until precipitation was complete. The diamide (1·65 g., 99%) had m. p. 237°, unchanged by recrystallisation from ethyl alcohol (Found: C, 25·3; H, 1·3; F, 53·3. Calc. for $C_6H_4O_2N_2F_8$: C, 25·0; H, 1·4; F, 52·75%). McBee, Wiseman, and Bachman (*loc. cit.*) recorded b. p. 70—71°/2·5 mm., n_D^{20} 1·3541, for the diester, and m. p. 237° for the diamide.

Analysis.—Carbon and hydrogen determinations were carried out by the method of Belcher

and Goulden (*Mikrochem. Mikrochim. Acta*, 1951, **36/37**, 679), fluorine determinations by the method of Belcher and Tatlow (*Analyst*, 1951, **76**, 593), and molecular-weight measurements by a modified Victor Meyer process.

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227. *Studies in Co-ordination Chemistry. Part XI.* New Types of Cuprous–Tertiary Arsine Complexes.*

By R. S. NYHOLM.

A series of cuprous complexes of methyldiphenylarsine has been prepared and their structures have been investigated. Four types, containing 1, 2, 3, and 4 molecules of the tertiary arsine to each molecule of cuprous halide have been isolated; examples of the last two types have not been reported previously. Complexes with the empirical formula $CuX,AsMePh_2$ (X = Cl,Br,I) are tetrameric, as earlier workers reported for the corresponding trialkylarsine derivatives. The structure of compounds with the empirical formula $CuX,2AsMePh_2$ cannot be decided with certainty without an *X*-ray crystallographic examination because on dissolution they undergo dissociation. From the method of preparation the structure in the solid state is probably $[Cu(AsMePh_2)_4][CuX_2]$, but the conductivity in nitrobenzene and molecular-weight measurements in benzene and nitrobenzene indicate that chiefly non-electrolytes are formed in solution. The new class of compounds with the empirical formula $CuX,3AsMePh_2$ are non-electrolytes containing four-covalent copper; these also dissociate in solution. Finally, compounds with the empirical formula $CuX,4AsMePh_2$ (X = I, ClO_4, NO_3) are shown to be salts in which X is the univalent anion; the perchlorate is a good conductor in nitrobenzene solution. The ease of dissociation of these compounds emphasises the need for caution when interpreting the results of many physical measurements on inorganic complexes in solution.

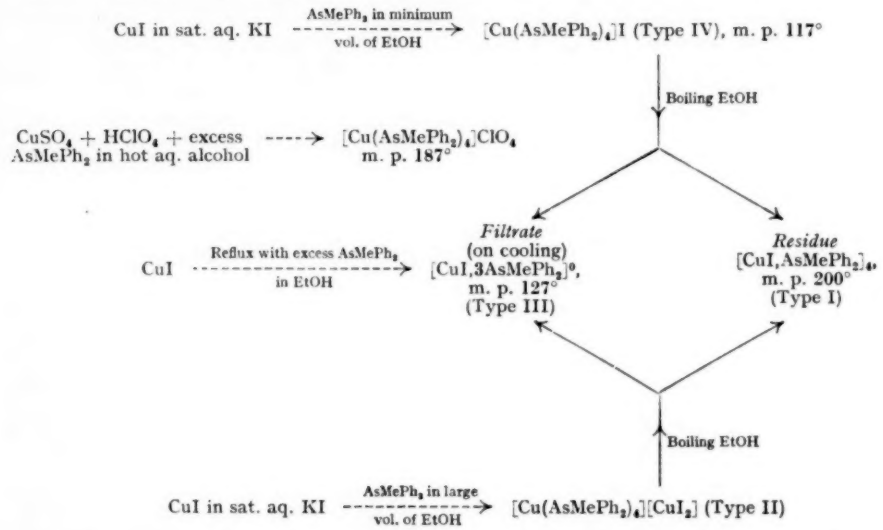
DURING a recent investigation of the structure of two apparently isomeric cuprous–cupric complexes of methyldiphenylarsine oxide (Part VIII, *J.*, 1951, 1767), it was found necessary to obtain more detailed information about the cuprous complexes of the tertiary arsine itself; the few data already available in the literature were insufficient for our purpose. The investigation of these cuprous complexes has led to the isolation of several compounds of a new and interesting type. This paper describes the preparation and properties of these compounds and discusses their dissociation phenomena.

Cuprous complexes of both methyldiphenylarsine ($AsMePh_2$) and dimethylphenylarsine ($AsMe_2Ph$) were first described by Burrows and Sandford (*J. Proc. Roy. Soc. N.S.W.*, 1935, **69**, 182). From methyldiphenylarsine these workers prepared a chloride, bromide, and nitrate to all of which the general formula $CuX,AsMePh_2$ was assigned; it was reported that all three were monomeric in freezing benzene. In addition, complexes of the empirical formula $CuX,2AsMe_2Ph$ were isolated with the other tertiary arsine but their molecular complexity was not investigated. The claim that the former compounds were monomeric was in marked contrast with the work of Mann, Purdie, and Wells (*J.*, 1936, 1503), who prepared and studied very thoroughly a series of cuprous iodide and cuprous bromide complexes of trialkylarsines and trialkylphosphines. All of these had the empirical formula $CuX,R_3As(P)$. From a study of their molecular weights in a variety of solvents, it was concluded that all the compounds were tetrameric; some dissociation occurred in solution

* Part X, *J.*, 1951, 3245.

but usually the association factor n in $[CuX,R_3As(P)]_n$ lay between 3·5 and 4·0. Using *X*-rays, Wells (*Z. Krist.*, 1937, **94**, 447) studied the crystal structure of the cuprous iodide–triethylarsine compound and confirmed that polymerisation to form a tetramer took place. Each cuprous atom is tetrahedrally co-ordinated, for in addition to each covalently bound iodine atom, each copper atom is attached to two other iodine atoms by co-ordinate links and to one triethylarsine molecule (cf. Fig. 1, *J.*, 1936, 1504; *Ann. Reports*, 1938, **35**, 158). No chloride compounds were described; also, the only complexes isolated contained one molecule of the ligand to each molecule of cuprous halide.

In this investigation it has been found that by suitably varying the method of preparation, and by utilising favourable solubility relationships, complexes containing 1, 2, 3, or 4 molecules of the tertiary arsine to each cuprous atom can be isolated; these will be designated in order as Types I, II, III, and IV. Examples of Types III and IV have not been isolated previously, and the structure of those of Type II had not hitherto been investigated. The preparation and relationships between the four types are conveniently described in terms of the iodides, even though one of the iodo-complexes, $CuI,2AsMePh_2$, could not be obtained in a pure state. However, the corresponding bis-arsine bromide and chloride are easily obtained free from impurity. Two of the compounds, $CuI,4AsMePh_2$ and $CuI,2AsMePh_2$, were obtained by treating the arsine with cuprous iodide dissolved in cold aqueous potassium iodide solution, and the other two, $[CuI,AsMePh_2]_4$ and $[CuI,3AsMePh_2]^0$, by the action of boiling alcohol upon the first two. As a modification, compounds of Type III can be prepared simply by heating under reflux an excess of the tertiary arsine in alcohol with the appropriate cuprous halide. The relations are summarised in the accompanying scheme.


CuI in sat. aq. KI
AsMePh2 in minimum vol. of EtOH
[Cu(AsMePh2)4]I (Type IV), m. p. 117°
Boiling EtOH
CuSO4 + HClO4 + excess AsMePh2 in hot aq. alcohol
[Cu(AsMePh2)4]ClO4 m. p. 187°
CuI
Reflux with excess AsMePh2 in EtOH
Filtrate (on cooling)
[CuI,3AsMePh2]0, m. p. 127° (Type III)
Residue
[CuI,AsMePh2]4, m. p. 200° (Type I)
Boiling EtOH
CuI in sat. aq. KI
AsMePh2 in large vol. of EtOH
[Cu(AsMePh2)4][CuI2] (Type II)

In Part VII (*J.*, 1951, 38) it was observed that when the ditertiary arsine chelate group, *o*-phenylenebisdimethylarsine, dissolved in a *small* volume of alcohol, was treated with potassium iodocuprite(I) in cold water the compound $[Cu(diarsine)_2]I$ was isolated. However, by using a *large* volume of alcohol, $[Cu(diarsine)_2][CuI_2]$ was obtained instead. From the earlier experience with the ditertiary arsine it seemed likely that *salts* were produced when methyldiphenylarsine reacted with potassium iodocuprite(I) in the cold; these then decompose in hot solution to yield non-electrolytes. The properties of all the compounds prepared are given in the table. All the molecular weights were determined cryoscopically, and the conductivities were measured in nitrobenzene solution. Since dissociation occurred in *freezing* benzene and nitrobenzene, no attempt was made to

determine any molecular weights ebullioscopically. The various chloride and bromide complexes were prepared in a similar manner to that given above, but it was not possible to isolate the compounds $[CuAs(MePh_2)_4]Cl$ and $[Cu(AsMePh_2)_4]Br$, probably owing to their greater solubility. Two other compounds of Type IV, $[Cu(AsMePh_2)_4]ClO_4$ and $[Cu(AsMePh_2)_4]NO_3$ were also prepared by the reducing action of excess of the tertiary arsine on the corresponding cupric salt in aqueous-alcoholic solution.

Structure and Properties.—Type I. Complexes of this type are clearly the methyldiphenylarsine analogues of the trialkylarsine complexes studied by Mann, Purdie, and Wells (*loc. cit.*). Molecular-weight measurements show that both the chloride and the bromide are polymerised in solution. Although the results are still less than those required for the tetramer in each case, this can be explained by partial decomposition in solution; with both the chloride and the bromide slow precipitation of the cuprous halide occurs during the measurement. Since each decomposing tetramer molecule produces *four* solute molecules in its place, a small amount of decomposition has a relatively large effect upon the observed molecular weight. The iodide was insufficiently soluble, both in benzene and in nitrobenzene, to permit a molecular-weight measurement in these solvents. In chloroform and bromoform decomposition appears to take place even more rapidly than in benzene and nitrobenzene. Our molecular-weight measurements do not agree with those of Burrows and Sandford (*loc. cit.*) but agree with the work of Mann, Purdie, and Wells (*loc. cit.*). However, it should be mentioned that the melting points which we observed are different from those reported by Burrows and Sandford (see p. 1258) and, therefore, it remains possible that these workers obtained isomeric two-covalent complexes. On the other hand, the extreme ease with which dissociation occurs in these compounds suggests that the compounds used may have been of mistaken identity. All three tetramers are poor conductors in nitrobenzene solution (see table, where Λ_m = molecular con-

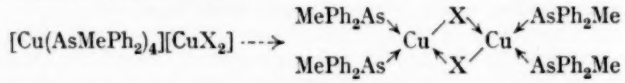
Type	Empirical formula	M. p.	Formula wt.	*M* in $PhNO_2$	Λ_m in $PhNO_2$ (M = formula wt.)	*M* in C_6H_6
I	$CuCl,AsR_3$	109°	343	>1205 [a] (1·75%)	0·3 ($4·5 \times 10^{-3}$M)	>1020 [a] (2·88%)
	$CuBr,AsR_3$	170	387·5	—	0·15 ($4·6 \times 10^{-3}$M)	>1260 [a] (1·74%)
	CuI,AsR_3	200	434·5	—	0·7 ($4·98 \times 10^{-3}$M)	—
II	$CuCl,2AsR_3$	127	587	626 (1·79%) 758 (2·84%)	1·5 ($10·4 \times 10^{-3}$M)	730 (2·98%)
	$CuBr,2AsR_3$	138	631·5	955 (1·68%)	0·35 ($13·8 \times 10^{-3}$M)	858 (3·63%)
	$CuI,2AsR_3$	?	678·5	—	—	—
III	$CuCl,3AsR_3$	117	831	502 (2·03%)	2·3 ($4·9 \times 10^{-3}$M)	795 (5·40%)
	$CuBr,3AsR_3$	134	875·5	778 (2·26%)	0·6 ($5·7 \times 10^{-3}$M)	580 (2·72%)
	$CuI,3AsR_3$	128	922·5	715 (1·74%) 721 (2·45%)	0·1 ($3·9 \times 10^{-3}$M)	549 (1·99%)
IV	$CuI,4AsR_3$	117	1166·5	—	—	—
	$CuClO_4,4AsR_3$	187	1139	545 (1·17%) 548 (2·46%)	24·4 ($3·9 \times 10^{-3}$M)	—
	$CuNO_3,4AsR_3$	115	1101·5	908 (1·61%)	4·3 ($4·47 \times 10^{-3}$M)	509 (3·41%) 542 (4·14%)

[a] In each of these measurements a little cuprous halide was precipitated during the determination. Since each act of decomposition produces a *greater* number of solute particles than the original number of tetramer molecules, the observed molecular weight is *smaller* than it would be if no decomposition had occurred.

ductivity); this confirms that they exist in solution as non-electrolytes and, taken together with molecular-weight measurements, supports the structures assigned. It is noteworthy that the compound $[CuCl,AsMePh_2]_4$ is the first example of a polymerised chloride with tertiary arsines to be described. However, Wilkins and Burkin (*J.*, 1950, 127) have shown that similar polymerisation to give the tetramer occurs when cuprous chloride is co-ordinated with one molecule of a long-chain amine.

Type II. The molecular-weight and conductivity measurements upon complexes of this type do not permit one to decide with any certainty the structure of this class of compound. From the method of preparation it is probable that in the solid state they are salts with the structural formula $[Cu(AsMePh_2)_4][CuX_2]$, but in solution they undergo extensive dissociation, forming non-electrolytes. The low conductivities in nitrobenzene (see table) could be explained by the following possible types of dissociation: (*a*) a mixture

of the two non-electrolytes $[CuX,3AsMePh_2]^0$ and $[CuX,AsMePh_2]_4$ is formed according to the reaction $4[Cu(AsMePh_2)_4][CuX_2] \dashrightarrow 4[CuX,3AsMePh_2]^0 + [CuX,AsMePh_2]_4$, or (*b*) a mixture of the tertiary arsine and the tetramer is produced according to the reaction $2[Cu(AsMePh_2)_4][CuX_2] \dashrightarrow [CuX,AsMePh_2]_4 + 4AsMePh_2$, or (*c*) a change into the halogen-bridged dimer occurs as follows :



Neither molecular-weight measurements nor preparative experience gives much support for (*c*), although this may occur to a limited extent in solution. For (*b*) one requires a molecular weight much smaller than that actually observed. Hypothesis (*a*) seems the most likely. However, it should be borne in mind that without definite evidence as to the nature of the actual species present in solution, all three (and possibly other) types of dissociation may occur to some extent. This dissolution of a salt in solvents such as benzene and nitrobenzene with the formation of non-electrolytes has been reported previously with this tertiary arsine. In Part II (*J.*, 1950, 848) it was shown that the compounds $[PtBr(AsMePh_2)_3]Br$ and $[PdBr(AsMePh_2)_3]Br$ dissolve readily in organic solvents, forming an equimolecular mixture of the tertiary arsine and the non-electrolytes $[PtBr_2,2AsMePh_2]^0$ and $[PdBr_2,2AsMePh_2]^0$. The ease with which such dissociations may be reversed was demonstrated by the fact that in acetone solution at low temperatures partial re-formation of the salt takes place, at least with the palladium complex. The essential point is that any conclusions which one may draw concerning the state of a complex in solution need not necessarily provide information concerning the structure of the substance in the solid state, particularly when one is dealing with a labile ligand such as methyldiphenylarsine.

Type III. These compounds appear to be the easiest to formulate, but again their behaviour in solution indicates considerable dissociation. The conductivities in nitrobenzene solution are all fairly small, showing that the products of dissociation are chiefly non-electrolytes, including possibly the tertiary arsine. The molecular weights in solution in all cases, both in benzene and in nitrobenzene, are less than those required for the simple tris-arsine non-electrolyte. It seems likely that the main dissociation is as follows : $4[CuX,3AsMePh_2]^0 \dashrightarrow [CuX,AsMePh_2]_4 + 8AsMePh_2$. Some support for this view is afforded by the fact that a suspension of the tetramer in benzene solution dissolves to a clear solution very easily on the addition of excess of tertiary arsine. Nevertheless, one might expect that the above dissociation would occur to only a limited extent since the tetramer itself is only slightly soluble in benzene. Only in the case of the chloride is the conductivity in nitrobenzene appreciable; this suggests that here, at least, noticeable amounts of the compound $[Cu(AsMePh_2)_4][CuCl_2]$ are formed in solution in this solvent. Compounds of this type have not been described previously. Mann, Purdie, and Wells mentioned the probability of their existence but the ligands used by these workers yielded only the tetramers. A major factor deciding whether they can be isolated with a particular tertiary arsine is undoubtedly the relative solubility of the different forms; although the tetramer is less soluble than the tris-arsine complex, in this instance the equilibrium can be forced to favour the formation of the latter by using a sufficient excess of the tertiary arsine.

Type IV. The physical properties of the iodide, $[Cu(AsMePh)_4]I$, could not be studied in much detail because the compound decomposed readily when treated with solvents. However, the corresponding perchlorate and nitrate were isolated and these have the properties typical of salts. A sulphate was also obtained but it is difficult to isolate in a pure state owing to its high solubility in aqueous alcohol. The perchlorate is readily soluble in nitrobenzene and the conductivity therein indicates a strong electrolyte. In Part VII (*loc. cit.*) it was shown that uni-univalent electrolytes of this kind usually have a molecular conductivity of the order of 20—30 mho in M/1000-solution; the conductivity of this perchlorate (see table) is in this range. The practically complete dissociation in nitrobenzene is confirmed by the molecular weight, which is about half of the formula weight, as expected. The compound is not sufficiently soluble in cold benzene to enable

a cryoscopic molecular-weight measurement to be done in this solvent. By a similar method of preparation to that used for the perchlorate, the nitrate $[Cu(AsMePh_2)_4]NO_3$ was prepared. This is readily soluble in alcohol and in organic solvents such as nitrobenzene, and benzene; however, it is one of the very few nitrates which are highly insoluble in water. The molecular weight in nitrobenzene is surprisingly high, suggesting that the compound is only dissociated to the extent of about 20% in this solvent. Since it is inconceivable that the cuprous atom is five-covalent, it is probable that ion-pair formation occurs to a large extent at the concentration used. This hypothesis is supported by the molecular conductivity in nitrobenzene solution; this is only about one-fifth of that usually observed for a fully ionised and dissociated electrolyte in this solvent. Taken together, these data indicate that very little, if any, dissociation to form $[CuNO_3,3AsMePh_2]^0$ and $AsMePh_2$ occurs in nitrobenzene solution. The molecular weight in benzene is surprisingly low, a value less than half of the formula weight being observed in two separate determinations. Since benzene is not as good an ionising solvent as nitrobenzene, it is apparent that considerable dissociation of a different kind is taking place. This must involve loss of tertiary arsine but the other products of dissociation are uncertain; they could be the non-electrolytes $[CuNO_3,3AsMePh_2]^0$ or $[CuNO_3,AsMePh_2]^0$. Burrows and Sandford claimed to have prepared the latter substance and stated that it was monomeric in benzene solution. Several attempts in these laboratories to repeat this preparation have been unsuccessful, the only compound which crystallises from solution being the tetra-arsine complex nitrate. All previous work on the chemistry of cuprous complexes shows that the metal atom is very reluctant to form covalent bonds with oxygen; whenever an oxy-anion is used the cuprous atom prefers to complete its four-fold co-ordination with less electronegative ligands while the anion is left with its negative charge, *e.g.*, in the compound $[Cu(ethylenethiourea)_4]NO_3$. However, the fact that complexes such as $[CuNO_3,3AsMePh_2]^0$ have not been isolated does not mean that they do not exist in solution, and the molecular-weight determination upon $[Cu(AsMePh_2)_4]NO_3$ is best understood if dissociation to form an equimolecular solution of $[CuNO_3,3AsMePh_2]^0$ and $AsMePh_2$ takes place. This hypothesis requires that benzene favours dissociation into non-electrolytes more than does nitrobenzene; in view of the difference in dielectric constants, this is not unreasonable. With neighbouring metals there is evidence that $-NO_3$ can be attached by covalent bonds. Thus the compound $[Ni(NO_3)_2,2PEt_3]^0$ was isolated by Jensen (*Z. anorg. Chem.*, 1936, **229**, 265) and shown to be monomeric in benzene solution. The large dipole moment (8·85 D) indicates either a *cis*-planar or a tetrahedral configuration; the magnetic moment (3·05 B.M.) points to the use of the higher $4s4p^3$ tetrahedral covalent bond orbitals rather than the lower $3d4s4p^2$ orbitals, which would result in a planar diamagnetic molecule. Cuprous copper is not isoelectronic with bivalent nickel but its tetrahedral complexes make use of the same bonding orbitals and there appears to be no fundamental theoretical objection to a complex of the type $[CuNO_3,3AsMePh_2]^0$ even though it has not been isolated.

All the compounds prepared are quite stable in air and except in the presence of moisture show no tendency towards oxidation. However, they are powerful reducing agents in solution and, with the exception of the nitrate and perchlorate, react instantly with silver nitrate in aqueous-alcoholic suspension to yield a mixture of metallic silver and the silver halide. The nitrate and perchlorate of course yield no silver halide.

As found in previous work, the results of this investigation are consistent with the view that a co-ordination number of four is displayed by cuprous copper whenever it is attached to tertiary arsines in cationic or non-ionic complexes. As is well known, the co-ordination number 2 occurs in anionic complexes such as the $[CuCl_2]^-$ ion. This is in keeping with the fairly general rule that metals which have more than one co-ordination number tend to show the maximum co-ordination number in cationic complexes, decreasing through non-ionic compounds to anionic complexes. The extent to which dissociation occurs in solution with these compounds makes other physical measurements difficult to interpret, and for this reason dipole-moment determinations, which were originally envisaged, were not carried out on these compounds. As this investigation was undertaken primarily in order to determine the stereochemistry of these substances no attempt has been made to study

the dissociation equilibria in solution in any detail. This might possibly be done by studying the ultra-violet absorption spectra of the various complexes, and of the free arsine itself, in solution. This problem will be examined, particularly in reference to the dissociation of the complex nitrate in benzene solution.

Experimental

Tetrakis[methyldiphenylarsinemonochlorocopper(I)].—Cuprous chloride (2·0 g., excess) was first freed from cupric salts by heating it with dilute alcoholic hydrochloric acid, followed by several washings, with alcohol. The cuprous salt was then heated under reflux for 30 minutes with methyldiphenylarsine (2·0 g.) in alcohol (75 ml.), and the solution filtered quickly at the pump. On rapid cooling, white crystals were obtained which were recrystallised from hot alcohol containing excess of cuprous chloride in suspension, the filtration and cooling being again rapid to prevent dissociation. The *compound* (1·4 g.) was obtained as a microcrystalline powder, m. p. 109° (Found : C, 45·9; H, 4·15; Cl, 10·3. $C_{52}H_{52}As_4Cl_4Cu_4$ requires C, 45·5; H, 3·79; Cl, 10·35%). When recrystallising the compound it is essential to redissolve it in alcohol in the presence of cuprous chloride and to filter and cool the solution rapidly, otherwise decomposition occurs yielding some of the trisarsine complex. The substance is soluble in benzene, chloroform, and nitrobenzene and slightly soluble in acetone, but in these solvents slow decomposition takes place with the precipitation of cuprous chloride. The compound is insoluble in water, ether, and light petroleum. Burrows and Sandford reported m. p. 104° for this compound.

Tetrakis(methyldiphenylarsine)copper(I) Dichlorocuprite(I).—Cuprous chloride (0·5 g.) was dissolved in a cold aqueous saturated solution of potassium chloride (20 ml.) containing 10N-hydrochloric acid (1 drop), and the solution warmed to 40°, and filtered into a stoppered flask. Methyldiphenylarsine (2·5 g.), dissolved in alcohol (20 ml.), was added, and the mixture well shaken for 10 minutes in an atmosphere of carbon dioxide. A white precipitate containing some potassium chloride appeared at once. Water (10 ml.) was added after 10 minutes to redissolve the potassium chloride, and the solution left for 24 hours with occasional shaking. The impure *dichlorocuprite* (2·8 g.) was then filtered off, well washed with alcohol and water, and recrystallised from cold benzene–light petroleum; it had m. p. 127° (Found : C, 53·0; H, 4·35; Cl, 5·9. $C_{52}H_{52}As_4Cl_2Cu_2$ requires C, 53·2; H, 4·45; Cl, 6·03%). The compound is readily soluble in chloroform, benzene, and nitrobenzene, and moderately soluble in acetone; it is insoluble in water, light petroleum, and cold alcohol but is decomposed by boiling alcohol.

Tris(methyldiphenylarsine)monochlorocopper(I).—Cuprous chloride (0·1 g.) was heated under reflux for 15 minutes with methyldiphenylarsine (0·8 g.) in alcohol (40 ml.), and the solution filtered hot and concentrated to 10 ml. On cooling, rhombic crystals (0·7 g.) separated. These were filtered off and recrystallised from a little alcohol containing a trace of arsine; m. p. 117° (Found : C, 56·35; H, 5·1; Cl, 4·2. $C_{39}H_{39}As_3ClCu$ requires C, 56·1; H, 4·7; Cl, 4·3%). The *compound* is readily soluble in benzene, acetone, and nitrobenzene, and very soluble in chloroform; it is insoluble in water and light petroleum.

Tetrakis[methyldiphenylarsinemonobromocopper(I)].—This compound can be prepared by treating $[Cu(AsMePh_2)_4][CuBr_2]$ with boiling alcohol; decomposition occurs and the tetramer remains insoluble while the tris-arsine bromo-complex passes into solution. It is more conveniently obtained as follows. Cupric bromide (1·1 g.) in alcohol (40 ml.) was heated to boiling and treated with methyldiphenylarsine (1·2 g.), the solution turning colourless immediately. Heating on the water-bath yielded white crystals; the solution was cooled, and the compound filtered off and well washed with alcohol. This was then treated with boiling alcohol twice in order to remove traces of the tris-arsine complex, leaving the substantially pure tetramer. To remove any cuprous bromide formed by decomposition, this was then dissolved in cold benzene, and the solution filtered and precipitated with light petroleum, giving a microcrystalline powder (1·0 g.) (Found : C, 40·6; H, 3·5. $C_{52}H_{52}As_4I_4Cu_4$ requires C, 40·3; H, 3·35%), m. p. 170° (Burrows and Sandford reported m. p. 133° for the substance which they described). The *compound* is soluble in benzene, chloroform, and nitrobenzene, and slightly soluble in acetone, some cuprous bromide being slowly deposited.

Tetrakis(methyldiphenylarsine)copper(I) Dibromocuprite(I).—Cuprous bromide (0·6 g.) was dissolved in a saturated aqueous solution of potassium bromide (15 ml.), and the solution filtered and treated in the cold with methyldiphenylarsine (1·25 g.) in alcohol (10 ml.). The mixture was well shaken for an hour in a stoppered flask in an atmosphere of carbon dioxide, a white precipitate of the required *dibromocuprite* being formed. This (1·6 g.) was filtered off,

well washed with saturated potassium bromide solution, then alcohol, and finally with water (Found: 49·95; H, 4·15; Br, 12·9. $C_{52}H_{52}As_4Br_2Cu_2$ requires C, 49·4; H, 4·1; Br, 12·7%). The compound is easily soluble in chloroform, benzene, acetone, and nitrobenzene.

Tris(methyldiphenylarsine)monobromocopper(I).—Cuprous bromide (0·3 g.) was heated under reflux with methyldiphenylarsine (1·8 g.) in alcohol (70 ml.) for several hours, most of the cuprous halide dissolving. At first a yellow insoluble compound was formed, probably $[CuBr,AsMePh_2]_4$, but if broken up this slowly dissolved on further refluxing. The solution was then filtered from traces of residue, and on cooling, sparkling white plates (1·4 g.) were obtained. The *compound* was filtered off, well washed with cold alcohol, and recrystallised from alcohol containing a little tertiary arsine; it had m. p. 134° (Found: C, 53·5; H, 4·55; Br, 9·4. $C_{39}H_{39}As_3BrCu$ requires C, 53·5; H, 4·45; Br, 9·2%), readily soluble in chloroform, nitrobenzene, acetone, and benzene. It may also be obtained from the filtrate when $[Cu(AsMePh_2)_4][CuBr_2]$ is boiled with alcohol.

Tetrakis[methyldiphenylarsinemonoiodocopper(I)].—The compound $[Cu(MePh_2As)_4]I$ (2·0 g.), prepared as below, was boiled with alcohol several times then filtered off at the pump; the tetra-arsine complex decomposed, yielding the required *tetramer* as a heavy, white, insoluble powder. This (1·1 g.) was washed many times with hot alcohol to remove any tris-arsine complex but it could not be recrystallised without some decomposition; it had m. p. 200° (Found: C, 35·7; H, 3·0; I, 29·7. $C_{52}H_{52}As_4I_4Cu_4$ requires C, 35·8; H, 3·0; I, 29·3%). The compound is soluble in chloroform and slightly soluble in nitrobenzene, cuprous iodide being slowly deposited; it is practically insoluble in benzene and other solvents.

Tris(methyldiphenylarsine)monoiodocopper(I).—This *compound* crystallised on cooling from the first filtrates of the above preparation of $[CuI,AsMePh_2]_4$. Recrystallised from an alcoholic solution containing a little tertiary arsine, it had m. p. 128° (Found: C, 50·9; H, 4·15; I, 13·6. $C_{39}H_{39}As_3ICu$ requires C, 50·8; H, 4·2; I, 13·8%). It may be prepared more conveniently in larger quantities by heating an alcoholic solution of excess of the tertiary arsine with cuprous iodide. The solution was filtered hot, and the required compound crystallised on cooling. Solubilities are similar to those of other tris-arsine complexes.

Tetrakis(methyldiphenylarsine)copper(I) *Monoiodide.*—Cuprous iodide (0·4 g.) was dissolved in a saturated aqueous potassium iodide solution (80 ml.) containing 10N-hydrochloric acid (1 drop), and the solution filtered. Methyldiphenylarsine (2·0 g.) was added but no visible reaction occurred before the addition of alcohol (5 ml.), after which a white precipitate appeared. The mixture was well shaken for 15 minutes, and the yellowish-white precipitate (2·3 g.) filtered off and well washed with potassium iodide solution, water, and dilute aqueous alcohol (Found: C, 52·8; H, 4·4. $C_{52}H_{52}As_4ICu$ requires C, 53·4; H, 4·5%). Further purification was difficult because the compound tends to lose some of the arsine very easily; the analysis indicates that some slight loss occurred during filtration. The complex dissolved in chloroform, nitrobenzene, and benzene but with decomposition; it had m. p. 117°.

Tetrakis(methyldiphenylarsine)copper(I) *Perchlorate.*—Copper sulphate pentahydrate (0·25 g.) in water (25 ml.) containing excess of perchloric acid was added to a solution of methyldiphenylarsine (1·5 g.) in alcohol (100 ml.) and water (50 ml. The mixture was heated on the water-bath for about an hour. Some white precipitate appeared at once and the blue colour gradually faded. The white, flaky, crystalline *perchlorate* was filtered off, washed many times with alcohol, and dried in a desiccator; its m. p. was 187° (1·05 g.) [Found: C, 55·0; H, 4·57; Cl(Carius), 2·8; Cu, 5·66. $C_{52}H_{52}As_4O_4ClCu$ requires C, 55·1; H, 4·55; Cl, 3·1; Cu, 5·58%]. The substance was insoluble in water and in organic solvents except nitrobenzene and hot benzene. Prolonged heating with concentrated nitric acid and aqueous silver nitrate did not yield any silver chloride, showing that all the halogen was present as the perchlorate ion. The compound was diamagnetic and, for the powder form at 21°, $\chi_g = -0{\cdot}45 \times 10^{-6}$.

Tetrakis(methyldiphenylarsine)copper(I) *Nitrate.*—Cupric nitrate hexahydrate (1·2 g.) in water (10 ml.) was treated with the tertiary arsine in excess (4·0 g.) in alcohol (70 ml.), and the solution heated on the water-bath for several hours. Aqueous alcohol was added gradually as the evaporation took place; the blue colour gradually decreased in intensity and white crystals were deposited. When the solution had become almost colourless, the *nitrate* was filtered off (3·0 g.) on cooling and well washed with aqueous alcohol; recrystallised from a small volume of alcohol, it had m. p. 115° (Found: C, 56·7; H, 4·8; N, 1·4. $C_{52}H_{52}As_4O_3NCu$ requires C, 56·7; H, 4·7; N, 1·3%). Unless water is added during the preparation of this compound, reduction to the cuprous state is very slow. The compound dissolves readily in benzene, chloroform, acetone, nitrobenzene, and even in alcohol. However, it is quite insoluble in water.

Conductivities were determined as in Part VIII (*loc. cit.*); magnetic susceptibility measurements were carried out as described in Part III (*J.*, 1950, 851). Molecular-weight measurements in nitrobenzene were determined by Roberts and Bury's method (*J.*, 1923, **123**, 2037); steady freezing points are obtained by adding excess of anhydrous sodium sulphate together with a drop of water, giving the constant aqueous vapour tension of the decahydrate.

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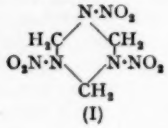
228. *The Heat of Nitrolysis of Hexamine in Nitric Acid.*

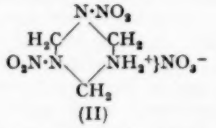
By W. J. DUNNING, B. MILLARD, and C. W. NUTT.

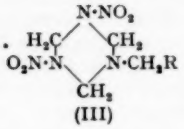
When hexamine is added to concentrated nitric acid, comparison of the rate of heat evolution with the rate of production of cyclonite (I) indicates the presence of an intermediate in the reaction. Nitrolysis with formation of two nitramino-groups occurs rapidly and the slow step is the conversion of this intermediate into cyclonite.

THE final product of the action of nitric acid on hexamine or its dinitrate at 0° is 1 : 3 : 5-trinitro-1 : 3 : 5-triaza*cyclo*hexane (hexahydro-1 : 3 : 5-trinitro-*s*-triazine; cyclonite; RDX) (I) (Henning, G.P. 104 280/1899; Herz, U.S.P. 1 402 695/1922; Hale, *J. Amer. Chem. Soc.*, 1925, **47**, 2754). At the time our investigations were carried out, no products other than (I) had been isolated from the nitrolysis mixture and no kinetic study of the reaction had been reported. By following the rates at which heat was evolved and supplementing these with rates at which (I) was produced, some insight into the mechanism of the reaction was obtained. A brief reference to the present results has already been made by Lamberton (*Quart. Reviews*, 1951, **5**, 95).

It was by no means certain at the time that hexamine and hexamine dinitrate followed the same reaction course, so hexamine was chosen for the rate studies, despite the disadvantage that a large temperature rise took place on its addition to nitric acid. In order to minimize this and the possible effects of reaction products (*e.g.*, water) on the rates, systems with the smallest practicable ratio of hexamine to nitric acid were studied. A lower limit on this ratio is placed by difficulties in the quantitative isolation of (I) from the mixture, which increase the smaller the ratio.


(I)


(II)


(III)

$NO_2{\cdot}NH{\cdot}CH_2{\cdot}N(NO_2){\cdot}CH_2{\cdot}NH_2,HNO_3$
(IV)

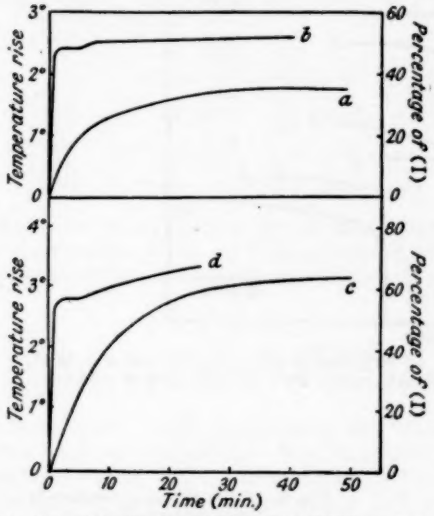
Results.—Rate of production of (I). The rates of formation of (I) are rapid at 20°, but become slower as the temperature and the concentration of acid are decreased. Fig. 1(*a*) shows the rate at which (I) is produced in 85% acid at 20°. Fig. 2 shows how the rate depends on acid concentration at 0°, and Fig. 3 how the rate is altered by the presence of potassium nitrate in 99·6% acid at −35·5°.

Rate of heat evolution. On addition of hexamine to nitrous-free nitric acid (80—100%), evolution of heat took place in two stages: a rapid evolution complete in less than one minute, followed by a slower evolution complete in times ranging from 5 minutes for 100% acid to one hour for 85% acid. The turning point, marking the end of the first rapid

evolution, was readily identifiable for 99% and weaker acids. For any particular acid concentration, the turning point became more distinct as the temperature was reduced until, at −35·5°, the second stage was completely suppressed and only the first stage remained. Fig. 4 shows some typical examples for 20°, 0°, and −35·5°.

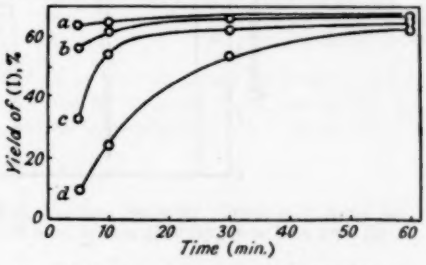
The amount of heat evolved at −35·5° per mole of hexamine in the first stage has been plotted against the acid concentration in Fig 5(*b*). A similar plot for 20° is not so curved

FIG. 1.



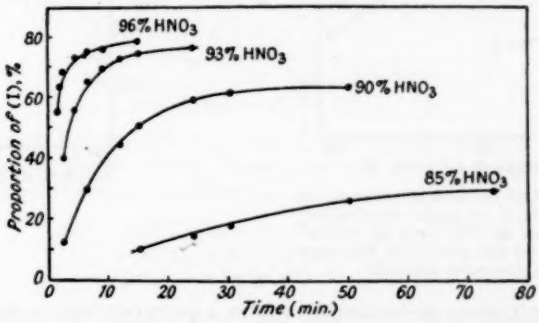
(*a*) *Rate of production of* (I) *in* 85% HNO_3 *at* 20°;
(*b*) *temperature rise in* 85% HNO_3 *at* 20°;
(*c*) *rate of production of* (I) *in* 90% HNO_3 *at* 0°;
(*d*) *temperature rise in* 90% HNO_3 *at* 0°.

FIG. 3. *Yield of* (I) *as a function of time (not corrected for solubility) in* 99·6% *acid at* −35·5°.



(*a*) *No added* KNO_3; (*b*) 5% KNO_3 *added*;
(*c*) 10% KNO_3 *added*; (*d*) 15% KNO_3 *added*.

FIG. 2. *Rates of production of* (I) *in* 96%, 93%, 90%, *and* 85% HNO_3 *at* 0°.



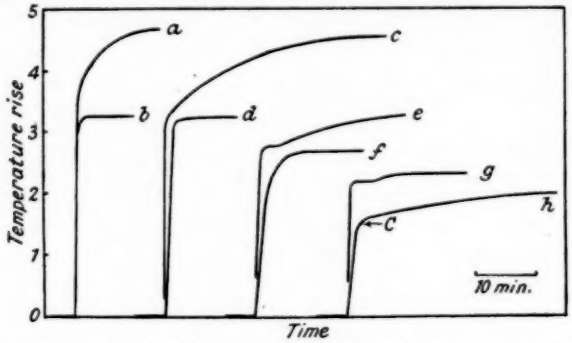
and is almost a straight line. On use of hexamine dinitrate, a curve [Fig. 5(*c*)] is obtained, which lies parallel to that for hexamine.

The total heat evolved in the first and second stages together at 20° is shown in Fig. 5(*a*).

Discussion.—Comparison of the rates of heat evolution and of the production of (I) (Fig. 1) shows that the latter is not associated with the first stage: this stage must indicate the formation of a precursor of (I), and Fig. 1 suggests the conditions favourable to the isolation of this precursor. Experiments directed to the isolation and characterisation of

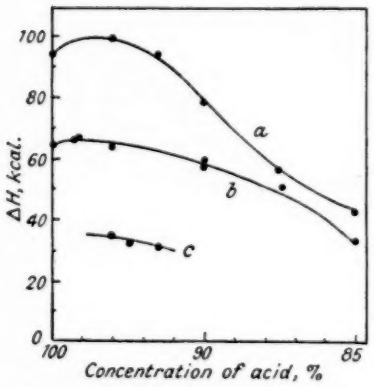
the precursor have already been reported (Vroom and Winkler, *Canadian J. Res.*, 1950, **28**, 701; Dunning and Dunning, *J.*, 1950, 2920, 2925, 2928; Burman, Meen, and Wright, *Canadian J. Chem.*, 1951, **29**, 767). Vroom and Winkler have isolated 3 : 5-dinitro-1 : 3 : 5-triaza*cyclo*hexane nitrate (II) and Dunning and Dunning have isolated a series of compounds, *e.g.*, 1-ethoxymethyl-3 : 5-dinitro-1 : 3 : 5-triaza*cyclo*hexane (III; R = OEt) from the reaction mixture. These observations, together with the rate of heat evolution,

FIG. 4. *Temperature rise as a function of time when hexamine is added to nitric acid.*



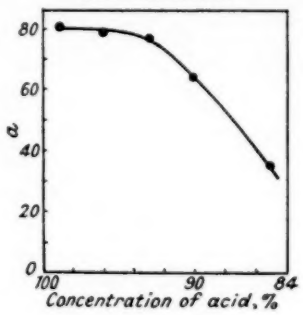
(*a*) 100% *Acid at* 20°; (*b*) 100% *acid at* −35·5°; (*c*) 96% *acid at* 20°; (*d*) 96% *acid at* −35·5°; (*e*) 90% *acid at* 0°; (*f*) 90% *acid at* −35·5°; (*g*) 85% *acid at* 20°; (*h*) 85% *acid at* −35·5°.

FIG. 5.



(*a*) *Total heat evolved per mole of hexamine at* 20° *as a function of acid concentration*; (*b*) *heat evolved in first stage at* −35·5° (*hexamine*); (*c*) *heat evolved in first stage at* −35·5° *for hexamine dinitrate.*

FIG. 6. *Value of* a *as a function of acid concentration.*



indicate that the nitrolysis of hexamine to form a precursor with a ring containing two nitramino-groups and one amino-group, occurs rapidly. The slow step in the kinetics is the formation of the third nitramino-group giving (I).

At −35·5° in 85% acid, the first stage of the heat evolution has itself become slower [Fig. 4(*h*)] and there is some indication of a resolution into a still earlier reaction. The amount of heat evolved in this earlier reaction (to point *C* in Fig. 4) is *ca.* 29 kcal., which is sufficiently close to the heat of formation of the dinitrate from hexamine and nitric acid (31 kcal.) to suggest that this earlier reaction is the formation of hexamine dinitrate in solution.

Our results indicate that the production x of (I) at 0° in 96, 93, 90, and 85% acids can be expressed empirically as a function of the time t by

$$x = a(1 - e^{-t/\tau}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where a and τ are constants depending on the strength of the acid (see table). Such an

Rate of production of (I)

Acid strength : Time, min.	99%	96%	93%	90%	85%	Acid strength : Time, min.	99%	96%	93%	90%	85%
1·5	—	55·7	—	—	—	30·0	—	—	—	62·0	18·3
2·0	—	64·0	—	—	—	50·0	80·5	—	—	63·9	26·2
2·5	66·9	68·7	40·9	13·3	—	74·0	—	—	—	—	29·17
4·5	—	74·1	56·2	—	—	100·0	—	—	—	—	33·0
6·5	70·2	75·3	65·8	30·5	—	120·0	—	—	—	—	32·6
9·0	—	—	70·1	—	—						
12·0	74·6	74·7	73·4	45·5	—	a	80·7	79·2	77·2	64·5	35·5
15·0	—	—	75·1	51·4	10·3	τ^{-1}	—	0·69	0·24	0·12	0·025
24·0	80·9	79·2	77·2	59·9	14·9	k_1	—	0·55	0·18	0·077	0·009

expression would result if the precursor were formed in amount a and underwent a first-order reaction to (I), or if the precursor were formed in constant yield (*ca.* 100%) and underwent first-order reactions, not only to (I), but to by-products A, B . . . as well :

$$\text{Precursor} \xrightarrow{k_1} \text{(I)}, \quad \text{Precursor} \xrightarrow{k_2} \text{A}, \quad \text{Precursor} \xrightarrow{k_3} \text{B} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The isolation of (IV) by Dunning and Dunning (*loc. cit.*) suggests that the by-products may be linear compounds. The heat evolved in the first stage shows a regular decrease with decreasing acid concentration (Fig. 5). This decrease could be explained as due to the varying heats of dilution of the acid with the reaction products, implying that the amount of precursor formed in each case is the same. On the other hand, the sharp decline in the value of a (Fig. 6) for acid concentrations between 90 and 85% suggest that in the lower acid strengths, some of the precursor is being destroyed by side reactions, giving products other than (I) (see 2).

If A is the amount of precursor initially formed and x, y, and z the amounts of (I), A, B, respectively, then

$$dx/dt = k_1(A - x - y - z)$$
$$dy/dt = k_2(A - x - y - z)$$
$$dz/dt = k_3(A - x - y - z)$$

whence

$$x = k_1A(1 - e^{-\Sigma kt})/\Sigma k \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Comparison of (3) with (1) gives Σk equal to τ^{-1}, and $k_1A/\Sigma k$ equal to a, from which k_1, the velocity constant for the conversion of precursor into (I), may be estimated (see table).

The following equilibria exist in nitric acid,

$$2HNO_3 \rightleftharpoons NO_2^+ + NO_3^- + H_2O$$
$$H_2O + HNO_3 \rightleftharpoons H_3O^+ + NO_3^-$$

and possibly

$$2HNO_3 \rightleftharpoons H_2NO_3^+ + NO_3^-$$

(Dunning and Nutt, *Trans. Faraday Soc.*, 1951, **47**, 15; Gillespie, Hughes, and Ingold, *J.*, 1950, 2552; Ingold and Millen, *J.*, 1950, 2612). The addition of water or potassium nitrate would suppress the dissociation into NO_2^+ and $H_2NO_3^+$. If one or both of these ions were the active agents in the nitrolysis, this would account for the rapid diminution of k_1 with decreasing acid concentration and for the effect of potassium nitrate on the rate of production (see Fig. 3). Since the addition of a small quantity of sulphuric acid to the nitric acid results in a reduced yield of (I), this may indicate that $H_2NO_3^+$, and not NO_2^+, is the nitrolytic agent concerned in the production of (I), though the loss in yield may be due to hydrolytic side reactions, enhanced by an increase in H_3O^+.

Experimental

Heat Evolution.—A cylindrical Dewar vessel formed the calorimeter, the inner portion being made from very thin " calorimeter " glass. The width of the short neck was half that of the main part of the vessel. Two lengthwise strips were left unsilvered so that the time of dissolution and any gas evolution during the reaction could be observed. The vacuum jacket was baked out *in vacuo*, gettered with cooled charcoal, and sealed off. Radiation losses were minimized by completely immersing the stoppered calorimeter in suitable temperature baths (20°, 0°, −35·5°) contained in larger Dewar flasks. Changes of temperature were observed with a standardised thermometer, readable to 0·01°. Through the stopper passed a stirrer driven by a motor, a funnel for inserting the hexamine, and a small hand-stirrer. The latter was constructed of thin glass tubing, and through the bottom ran a spiral nichrome wire by means of which electrical energy could be introduced into the calorimeter. The calorimeter constant was determined at 20° and Miscenko's values (Landolt–Börnstein " Tabellen," IIb, p. 1657) for the specific heats of the various concentrations of nitric acid were used. At −35·5°, the thermal capacities of the calorimeter and of the acid contained in it were determined for each experiment.

The appropriate acid (150 c.c.) was pipetted into the calorimeter. When the temperature had reached constancy, hexamine (0·714 g.) or hexamine dinitrate (1·3566 g.) was dropped in. Temperature readings were taken every 10 seconds for 10 minutes and then at suitable intervals until the temperature was again stationary.

In the experiments at 20°, it was found that the second part of the heat evolution was sensitive to the nitrous acid content, though the first portion was not affected. The nitrous acid was destroyed by adding a small quantity of urea (0·6 g. per 200 g. of acid) to the acid and leaving the whole overnight; the results obtained were then reproducible and, for 96% and 85% concentrations, agreed with those obtained with carefully distilled and carefully diluted acids. The effect of nitrous acid at −35° was not noticeable, and treatment with urea was not necessary.

Rate of Production of (I).—In investigating the effect of acid concentration on rates, there are several points to consider. The nitrolysis produces water, besides other products, and this will affect the acid concentration in the later stages of the reaction. Prof. H. D. Springall and Dr. E. Roberts (private communication) have measured the amount of water produced by means of the Karl Fischer reagent and this corresponds to 3 moles of water per mole of hexamine. However, the rate of production of (I) is followed by diluting the acid and allowing (I) to crystallise. Some of (I) remains in solution and difficulties of quantitative isolation become serious if the hexamine : acid ratio is reduced too far. The ratio chosen was 1 : 100 (w/w); at this ratio, the water produced by the nitrolysis would decrease the acid concentration by 0·4%. The effect which the basic hexamine has upon the acid dissociation in the early stages is also reduced by choosing a low ratio. Further control tests on (I) showed that, over the periods of the nitrolyses, there was no significant destruction of (I) in the different acids.

A quantity of 99% acid was divided into about 30 portions of 200 g., each portion being used for a single measurement. The procedure is described for the 99% series and the 85% series. In the former, 99% acid (200 g.) was cooled to a predetermined extent below 0° and finely crushed hexamine (2 g.) was added at once to the vigorously stirred acid in a thin-walled flask; the temperature rose rapidly (<30 sec.) to 0°. The mixture was immediately placed in a thermostat at 0°, and after the appropriate time intervals, it was poured into water (1000 c.c.), and more water (200 c.c. exactly) added as washings from the reaction vessel. After being stirred, the diluted mixture was transferred to a thermostat at 20° and left for 24 hours. The crystalline precipitate was collected on a sintered filter and washed with 5 c.c. of ice-cold water. The filter was heated in an air-oven at 100°, cooled, the contents damped with water, and the filter reheated. After cooling, the contents were washed with 5 c.c. of ice-cold water. This procedure hydrolyses any linear compounds, but has no effect on (I). The filter was then weighed.

For the 85% series, the 99% acid (200 g.) was divided into two portions; one portion (170 g.) was diluted with water (30 g.) and used for the nitrolysis, the other (30 g.) being added to the water (1000 c.c.) to be used later as the diluent of the reaction mixture. The procedure was then the same as for the 99% acid. This method ensures that the concentration of the nitric acid in the resultant diluted reaction mixture is exactly the same for all the series of determinations and hence any correction for solubility of (I) in the diluted mixtures is always the same.

The solubility of (I) in the diluted mixture was determined by carrying through the pro-

cedure for the nitrolysis, but using (I) instead of hexamine, and determining the amount recovered. The loss was found to correspond to 7·0% on the yield.

The yields of (I) plus 7% constitute the amount produced; these are illustrated in Fig. 2. From the gradients of the curves, a value for the yield a at infinite time (zero rate) was obtained. By use of these final values of a, log $(a - x)$ was plotted against time and, for all acid concentrations except 99%, good straight lines were obtained, the gradients of which gave the time constant τ. The values of a and τ^{-1} are given in the table, and the curves drawn in Fig. 2 correspond to these values.

The authors are indebted to Dr. E. Roberts, of the Ministry of Supply, for many helpful discussions.

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229. *Substituted Benzidines and Related Compounds as Reagents in Analytical Chemistry. Part IX.* Naphthidine- and 3 : 3′-Dimethylnaphthidine-sulphonic Acids as New Redox Indicators.*

By R. BELCHER, A. J. NUTTEN, and W. I. STEPHEN.

Sulphonic acid derivatives of naphthidine and 3 : 3′-dimethylnaphthidine have been prepared, and their properties as indicators examined in the titration of cadmium and zinc with ferrocyanide, ferrous salts with dichromate and with ceric sulphate, and vanadic acid with ferrous salts.

IT was shown in previous communications that naphthidine (Belcher and Nutten, *J.*, 1951, 548) and 3 : 3′-dimethylnaphthidine (Belcher, Nutten, and Stephen, *J.*, 1951, 1520) could be used as internal indicators in the titration of zinc with ferrocyanide. The application of 3 : 3′-dimethylnaphthidine was later extended to the titration of cadmium, calcium, and indium with ferrocyanide (Belcher, Nutten, and Stephen, Part VIII, *loc. cit.*). The strongly polar sulphonic acid group has now been introduced into the molecules of both compounds and the indicator properties of the resulting sulphonic acids have been examined. These compounds form water-soluble alkali salts; they can be used in redox titrations other than that employing the ferrocyanide–ferricyanide system, and the end-points are less sluggish than those of the free bases. The present paper describes the preparation and properties of these sulphonic acids and their use as indicators in the titration of zinc and cadmium with ferrocyanide, vanadic acid with ferrous iron, and ferrous iron with dichromate and ceric sulphate.

The Sulphonation of Naphthidine and 3 : 3′-Dimethylnaphthidine and the Properties of the Resulting Compounds.—When naphthidine and 3 : 3′-dimethylnaphthidine were treated with warm (*ca.* 40°) fuming sulphuric acid, some decomposition was observed; pale brown solids separated when the solution was poured on crushed ice. Both substances were soluble in sodium carbonate or other alkalis and were precipitated by the addition of dilute sulphuric acid. When this precipitation was carried out two or three times, white, amorphous substances were obtained. Sulphonation of the diacetyl derivatives under the same conditions gave identical products but in smaller yield. Analysis of the product obtained by the sulphonation of naphthidine corresponded to that of a monosulphonic acid sulphate, whereas that from 3 : 3′-dimethylnaphthidine gave a value for a disulphonic acid sulphate. In the case of naphthidine, less vigorous sulphonation provided mixtures of mono- and di-sulphonic acids, and with both diamines, similar conditions led to decreased yields of sulphonic acids. When more vigorous sulphonation was used, especially with chlorosulphonic acid, yields were again decreased owing to increased decomposition of the diamines.

The orientation of the sulphonic acid groups in the molecules is not known. If it were assumed that the oxidation of these substances results in the formation of meriquinoid

* Part VIII, *J.*, 1951, 3444.

compounds, then the substitution could not occur at the 2-position because of the steric effect of the bulky sulphonic acid groups. As both sulphonic acids are readily oxidised to intensely coloured substances, it may be taken as evidence that the sulphonic acid groups are situated in the unsubstituted 6- or 7-positions, which would provide likely sites for attack by the sulphuric acid. The final preparations adopted are described later.

Indicator Properties.—In the presence of oxidising agents, and in acid solution, naphthidinesulphonic acid is converted into a bright red compound, and 3 : 3′-dimethylnaphthidinedisulphonic acid into an intense red-violet compound. The colours given by the sulphonic acids were brighter than those given by the free bases. The relative stabilities of the oxidised indicators showed that naphthidinesulphonic acid was rapidly destroyed. Sensitivities towards oxidising agents could not therefore be determined satisfactorily. 3 : 3′-Dimethylnaphthidinedisulphonic acid, however, in the oxidised form was stable during several hours, and it had been shown previously that the free base was stable for almost 3 days. The sensitivities of 3 : 3-dimethylnaphthidinedisulphonic acid towards selected oxidants are included in the table on p. 1272. The sensitivities of naphthidine and 3 : 3′-dimethylnaphthidine have been determined by Belcher, Nutten, and Stephen (*Analyst*, 1951, **76**, 378, 430). Thus sulphonation of naphthidine gave a compound with indicator properties but of little practical application; on the other hand, 3 : 3′-dimethylnaphthidinedisulphonic acid appeared to have possible applications.

Titration of Zinc with Ferrocyanide.—A comparative examination of naphthidine, 3 : 3-dimethylnaphthidine, naphthidinesulphonic acid, and 3 : 3′-dimethylnaphthidinedisulphonic acid was made in the titration of zinc with ferrocyanide. All four indicators gave sharp end-points in this titration. 3 : 3′-Dimethylnaphthidinedisulphonic acid was better than 3 : 3-dimethylnaphthidine in that it gave an instantaneous change at the end-point, enabling the more rapid direct titration procedure to be employed in place of the back-titration technique necessarily used with the free base. Solutions of 0·001M-zinc could readily be titrated as with the free base. Naphthidine gave sharp end-points with solutions not more dilute than 0·01M-zinc. The procedure employed was similar to that described in Part VII (*J.*, 1951, 1520). Results were also checked by the back-titration procedure. Naphthidinesulphonic acid offered no advantage over its homologue. Although it afforded sharp end-points in 0·05M-solutions, the colour change of grey to brownish-red was not as favourable as the green to deep reddish-purple of the dimethyl compound. It proved of little use when solutions more dilute than 0·01M-zinc were titrated. The behaviours of all four indicators for this titration are summarised below.

Indicator	End-point change	Comments
3 : 3′-Dimethylnaphthidine-disulphonic acid	Green to deep red-dish-purple	End-points sharp in *direct* titration at all concentrations
3 : 3′-Dimethylnaphthidine	Grey-green to purple-red	End-points sharp in *back*-titration at all concentrations
Naphthidinesulphonic acid	Grey to brown-red	End-points sharp in *direct* titration when zinc concentration not less than 0·01M
Naphthidine	Grey-green to pink-red	End-points sharp in *back*-titration when zinc concentration not less than 0·01M

Titration results for 3 : 3′-dimethylnaphthidinedisulphonic acid are included in the tables. No indicator correction is necessary.

Titrations with 0·05M-zinc solutions.

0·05M-Zn taken (ml.)	0·025M-$K_4Fe(CN)_6$ added (ml.)		0·025M-$K_4Fe(CN)_6$, calc. (ml.) †	Back titrn.: 0·05M-Zn (ml.)	Total 0·05M-Zn consumed (ml.): ‡	
	(*a* *)	(*b* *)			Found	Calc.
25	33·32	40	33·33	4·98	29·98	30·00
25	33·34	40	33·33	5·00	30·00	30·00
20	26·65	30	26·67	2·48	22·48	22·50
20	26·65	30	26·67	2·50	22·50	22·50
15	20·00	25	20·00	3·75	18·75	18·75
15	19·98	25	20·00	3·76	18·76	18·75
10	13·34	15	13·33	1·24	11·24	11·25
10	13·32	15	13·33	1·26	11·26	11·25
5	6·64	7·5	6·67	0·64	5·64	5·63
5	6·68	7·5	6·67	0·62	5·62	5·63

Titrations with 0·005M-*zinc solutions.*

0·005M-Zn taken (ml.)	0·0025M-$K_4Fe(CN)_6$ added (ml.)		0·0025M-$K_4Fe(CN)_6$, calc. (ml.) †	Back titrn.: 0·005M-Zn (ml.)	Total 0·005M-Zn consumed (ml.): ‡	
	(*a* *)	(*b* *)			Found	Calc.
20	26·64	30	26·67	2·52	22·52	22·50
20	26·66	30	26·67	2·49	22·49	22·50
15	20·02	25	20·00	3·71	18·71	18·75
15	20·02	25	20·00	3·73	18·73	18·75
10	13·32	15	13·33	1·23	11·23	11·25
10	13·30	15	13·33	1·20	11·30	11·25
5	6·75	10	6·67	2·47	7·47	7·50
5	6·73	10	6·67	2·49	7·49	7·50

Titrations with 0·001M-*zinc solutions.*

0·001M-Zn taken (ml.)	0·0005M-$K_4Fe(CN)_6$ added (ml.)		0·0005M-$K_4Fe(CN)_6$, calc. (ml.) †	Back titrn.: 0·001M-Zn (ml.)	Total 0·001M-Zn consumed (ml.): ‡	
	(*a* *)	(*b* *)			Found	Calc.
15	20·04	25	20·00	3·72	18·72	18·75
15	20·06	25	20·00	3·73	18·73	18·75
10	13·36	15	13·33	1·22	11·22	11·25
10	13·34	15	13·33	1·23	11·23	11·25
5	6·71	10	6·67	2·48	7·48	7·50
5	6·70	10	6·67	2·51	7·51	7·50

* Column (*a*) gives values of $K_4Fe(CN)_6$ obtained in the direct titration; col. (*b*) gives the total amount of $K_4Fe(CN)_6$ added. † Cf. col. (*a*). ‡ Cf. $\frac{3}{4}$ × col. (*b*).

Titration of Cadmium with Ferrocyanide.—Naphthidinesulphonic acid and 3 : 3′-dimethylnaphthidinedisulphonic acid were employed as indicators in the titration of cadmium solutions, under the conditions described in the previous communication. With naphthidinesulphonic acid the colour change was not as intense as that of 3 : 3′-dimethylnaphthidinedisulphonic acid. End-points were sharp with both indicators but the latter was the better. In the direct titration, equilibrium was rapidly attained at the end-point with both indicators. There was little to choose between 3 : 3-dimethylnaphthidine and its sulphonic acid, but the latter gave a redder, brighter colour at the end-point. Results for 0·05M- and 0·01M-cadmium solutions with the disulphonic acid as indicator are tabulated below.

Titrations with 0·05M-*cadmium solutions.*

0·05M-Cd taken (ml.)	0·05M-$K_4Fe(CN)_6$ added (ml.): Found	Calc.
25	19·98, 20·00, 20·00	20·00
20	15·98, 15·96, 16·02	16·00
15	12·01, 11·98, 12·00	12·00
10	8·02, 8·02, 8·00	8·00
5	4·01, 4·00, 4·03	4·00

Titrations with 0·01M-*cadmium solutions.*

0·01M-Cd taken (ml.)	0·01M-$K_4Fe(CN)_6$ added (ml.): Found	Calc.
25	20·01, 20·02, 19·98	20·00
20	15·96, 16·02, 16·00	16·00
15	12·02, 11·97, 12·00	12·00
10	8·01, 7·98, 7·98	8·00
5	3·96, 4·01, 3·97	4·00

Titration of Ferrous Salts with Dichromate.—Straka and Oesper (*Ind. Eng. Chem. Anal.*, 1934, **6**, 405) have recommended naphthidine as an internal indicator in the titration of ferrous iron with potassium dichromate. The red colour of the oxidised base is discharged by ferrous ions, the colour change being reversible. However, the colour change is slow and the indicator is partly destroyed. 3 : 3′-Dimethylnaphthidine also changes very slowly, but no destruction of this indicator is apparent.

Naphthidine- and 3 : 3′-dimethylnaphthidine-sulphonic acids are better indicators for this titration although the end-points are not as sharp as those given by diphenylaminesulphonic acid. Satisfactory results have been obtained for ferrous iron by using procedures commonly recommended. Phosphoric acid or ammonium fluoride must be present to form a complex with excess of ferric ions. Titration results for 0·1N- and 0·01N-solutions are included in the tables.

Titrations with 0·1N-*dichromate solutions.*

0·1N-Fe^{2+} taken (ml.)	0·1N-$K_2Cr_2O_7$ added (ml.): Found	Calc.
25	24·98, 25·01, 24·98	25·00
20	19·96, 19·99, 20·01	20·00
15	15·02, 15·00, 15·00	15·00
10	9·97, 9·98, 9·98	10·00
5	5·01, 5·00, 5·02	5·00

Titrations with 0·01N-*dichromate solutions.*

0·01N-Fe^{2+} taken (ml.)	0·01N-$K_2Cr_2O_7$ added (ml.): Found	Calc.
25	25·01, 24·99, 24·98	25·00
20	20·02, 20·00, 20·00	20·00
15	14·98, 14·98, 15·00	15·00
10	9·99, 9·97, 10·01	10·00
5	5·02, 5·00, 5·02	5·00

Titration of Vanadic Acid with Ferrous Iron.—The action of naphthidine- and 3 : 3′-dimethylnaphthidine-sulphonic acids was investigated in the direct titration of vanadate solutions with ferrous salts. Although the indicator change was slow, satisfactory results were obtained when sufficient phosphoric acid or ammonium fluoride was present as above. The end-point change was from the red or red-violet colours of the oxidised indicators to the pale blue colour of the vanadyl ion. 3 : 3′-Dimethylnaphthidinedisulphonic acid was more stable than naphthidinesulphonic acid; the latter indicator was added near the end-point as the high concentrations of vanadic acid rapidly caused its destruction. Apart from its stable oxidation colour in vanadate solutions, 3 : 3′-dimethylnaphthidinedisulphonic acid had no advantage over diphenylaminesulphonic acid in this titration. Tungstic acid did not interfere; no indicator correction was necessary. Titration results for 0·1N- and 0·01N-vanadate solutions follow.

Titrations with 0·1N-*vanadate solutions.*

0·1N-VO_3^{1-} taken (ml.)	0·1N-Fe^{2+} added (ml.): Found	Calc.
25	24·98, 24·96, 15·01	25·00
20	19·96, 19·98, 20·00	20·00
15	15·02, 15·00, 15·00	15·00
10	10·02, 9·98, 9·99	10·00
5	4·98, 5·01, 5·01	5·00

Titrations with 0·01N-*vanadate solutions.*

0·01N-VO_3^{1-} taken (ml.)	0·01N-Fe^{2+} added (ml.): Found	Calc.
25	25·02, 25·00, 24·98	25·00
20	19·98, 20·00, 19·97	20·00
15	15·02, 15·02, 15·01	15·00
10	9·96, 9·98, 9·96	10·00
5	4·97, 5·01, 5·00	5·00

Titration of Ferrous Iron with Ceric Sulphate.—The sulphonic acid indicators were of no value in this titration. The end-points obtained were too sluggish even when sufficient phosphoric acid was present, and were markedly inferior to those obtained with ferrous 1 : 10-phenanthroline. Their use with ceric sulphate was not further investigated.

The Sensitivity of 3 : 3′-*Dimethylnaphthidinedisulphonic Acid towards Selected Oxidising Agents.*—The sensitivity of this acid towards various oxidising agents which readily produced the characteristic red-purple colour in acid solution was determined. The results are given below, the colours obtained being stable over a considerable period. In no case did the sensitivity exceed that of the parent base although comparable results were obtained with VO_3^{1-} and $Fe(CN)_6^{3-}$. Analogous experiments with naphthidinesulphonic acid showed that it was too insensitive for any measurements to be taken.

Ion	Ce^{4+}	$Cr_2O_7^{2-}$	VO_3^{1-}	$Fe(CN)_6^{3-}$, Zn^{2+}	IO_4^{1-}
Limit of identification, μg.	0·5	0·2	0·1	0·1	0·1
Concn.	$1:4\times10^5$	$1:1\times10^6$	$1:2\times10^6$	$1:2\times10^6$	$1:2\times10^6$

Experimental

A. *Preparation of Naphthidine- and* 3 : 3′-*Dimethylnaphthidine-sulphonic Acids.*—Naphthidine (4 g.) was refluxed for 1 hour with a slight excess of acetic anhydride containing a small amount of concentrated sulphuric acid, and the product poured into water. The solid, brown diacetyl derivative was filtered off, washed well with water, and recrystallised from aqueous alcohol; yield theoretical.

This diacetyl compound (5 g.) was added in small quantities to fuming sulphuric acid (10 ml.) at 5°. The resulting liquid was vigorously stirred and slowly warmed on the water-bath to 40°, kept at this temperature for 1 hour with constant stirring, and then poured on crushed ice (100—150 g.). The solution was boiled under reflux for ½ hour. After cooling, the brown solid was filtered off and washed with a little water. The crude sulphonic acid was dissolved in a slight excess of aqueous ammonia, and the solution boiled (charcoal) and filtered. Dilute

sulphuric acid was added, and the resulting sulphate of naphthidinesulphonic acid was filtered off. This process was repeated twice to give a colourless amorphous substance in 50% yield (Found: C, 52·15; H, 3·6; N, 5·8; S, 13·5. Calc. for $C_{20}H_{16}O_3N_2S,H_2SO_4$: C, 51·9; H, 3·9; N, 6·1; S, 13·9%).

An identical procedure applied to 3 : 3′-dimethylnaphthidine afforded similarly a white substance in 60% yield (Found: C, 46·3; H, 3·8; N, 4·8; S, 16·6. Calc. for $C_{22}H_{20}O_6N_2S_2,H_2SO_4$: C, 46·3; H, 3·9; N, 4·9; S, 16·9%).

B. *Solutions required.—Zinc sulphate*: 0·05, 0·005, and 0·001M. The 0·05M-solution was prepared by dissolving 3·269 g. of pure zinc in a slight excess of dilute sulphuric acid and dilution to 1 l. with water. The more dilute solutions were obtained by appropriate dilution of this solution, the concentration of which was checked by determining the zinc by precipitation with 8-hydroxyquinoline.

Cadmium sulphate: 0·05 and 0·01M. The 0·05M-solution was prepared by dissolving recrystallised A.R. cadmium sulphate in water and dilution to 1 l. The solution was standardised by determining the cadmium by precipitation with 8-hydroxyquinoline.

Potassium ferrocyanide: 0·05, 0·025, 0·0025, and 0·0005M. The 0·05M-solution was prepared by dissolving 21·102 g. of A.R. potassium ferrocyanide trihydrate and about 0·5 g. of sodium carbonate in water and dilution to 1 l. This solution was standardised by titration with a standard zinc solution, 3 : 3′-dimethylnaphthidine being used as indicator. The trihydrate was obtained by recrystallising pure potassium ferrocyanide and drying it to constant weight over a saturated solution of sodium chloride and sucrose. The weaker solutions were prepared from the 0·05M-solution by appropriate dilution.

Potassium ferricyanide: 1, 0·2, and 0·1%. The pure salt was dissolved in water and stored in a dark bottle. The solution was prepared fresh each day.

Ferrous ammonium sulphate: 0·1 and 0·01N. The 0·1N-solution was prepared by dissolving 39·215 g. of A.R. ferrous ammonium sulphate in water containing 10 ml. of concentrated sulphuric acid and diluting it to 1 l. The solution was standardised against potassium dichromate, with barium diphenylaminesulphonate as indicator.

Potassium dichromate: 0·1 and 0·01N. The 0·1N-solution was prepared by dissolving 4·904 g. of A.R. potassium dichromate in water and diluting it to 1 l.

Ammonium vanadate: 0·1 and 0·01N. The 0·1N-solution was prepared by dissolving 10·7 g. of pure ammonium metavanadate in dilute sulphuric acid and diluting it to 1 l. with water. The solution was standardised by reduction of the vanadic acid with sulphur dioxide and titration of the vanadyl solution with potassium permanganate.

Ceric sulphate: 0·1 and 0·01N. An approximately 0·5N-solution of ceric sulphate was prepared by dissolving 35 g. of purest anydrous ceric sulphate in 25 ml. of 1 : 1-sulphuric acid with warming and frequent additions of water until all the salt was dissolved. This solution was diluted to 1 l. with water, and its exact concentration determined by titration with standard ferrous ammonium sulphate, ferrous 1 : 10-phenanthroline indicator being used. The 0·1 and 0·01N-solutions were obtained by appropriate dilution of the stock 0·5N-solution.

Indicator Solutions.—Naphthidinesulphonic and 3 : 3′-dimethylnaphthidinedisulphonic acid. 1 G. of the acid was dissolved in a slight excess of aqueous ammonia and boiled to expel the excess. The resulting solution was diluted to 100 ml.

Naphthidine and 3 : 3′-dimethylnaphthidine. 1 G. of base was dissolved with warming in 100 ml. of glacial acetic acid.

Titration of Zinc.—0·05M-Solutions. The zinc test solution was made about 1N with respect to sulphuric acid in a volume of 50 ml., and 10% ammonium sulphate added to give a concentration of 1 g. in 50 ml. Four drops of 1% potassium ferricyanide and 2 drops of indicator were added, and the solution was titrated with potassium ferrocyanide until the addition of one drop of ferrocyanide caused the colour change given (in reverse) on p. 1270. A 10—20% excess of ferrocyanide was then run in, and the solution titrated with standard zinc solution to the respective indicator changes.

0·005M-Solutions. The above procedure was repeated except that the final concentration of sulphuric acid in 50 ml. was reduced to 0·2N and that of ammonium sulphate to 0·4%. Four drops of 0·2% potassium ferricyanide and 2 drops of indicator were added, and the titration carried out as above.

0·001M-Solutions. In this case the final concentration of sulphuric acid in 50 ml. was 0·1N and that of ammonium sulphate was 0·2%. Four drops of 0·1% potassium ferricyanide and 2 drops of indicator were added.

Titration of Cadmium.—To the neutral cadmium test solution 10 ml. of 10% ammonium

sulphate were added, and the volume was adjusted to 40—50 ml. with water. Two drops of 1% potassium ferricyanide and 2 drops of indicator were added. The solution was titrated with potassium ferrocyanide until the colour changed from red-brown or red-violet, depending on the indicator, to greenish-white.

Titration of Ferrous Iron with Potassium Dichromate.—The ferrous test solution was acidified with 10 ml. of a 1 : 1 mixture of concentrated sulphuric and phosphoric acids in a volume of 150 ml. Four drops of indicator were added. Potassium dichromate was run in from a burette, rapidly at first, then more slowly as the end-point was approached. The solution was vigorously shaken and dichromate added drop-wise until a permanent colour change to red or red-purple was obtained.

Titration of Vanadic Acid with Ferrous Iron.—The test solution was acidified and diluted as above. Four drops of indicator were added and the solution titrated with ferrous ammonium sulphate to the first permanent pale blue. When tungstic acid was present, 10 ml. of 5% ammonium fluoride and 10 ml. of 50% sulphuric acid were added in place of the phosphoric–sulphuric acid mixture and the solution was titrated immediately.

Titration of Ferrous Iron with Ceric Sulphate.—The ferrous test solution was acidified with sulphuric acid and various amounts of phosphoric acid or ammonium fluoride were added, followed by 4 drops of indicator, and the solution was titrated with ceric sulphate solution.

Sensitivity Determinations.—One drop of the ion test solution was placed in a depression on a spot plate; one drop of 1N-sulphuric acid and one drop of indicator solution were added. The procedure was repeated with more dilute test solutions until the red-purple colour was just observed. Each test was allowed to stand for 30 sec. for full development of the colour to be obtained.

Thanks are due to Mr. B. S. Stringer for microanalysis of the compounds.

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Edgbaston, Birmingham, 15. [*Received, October 3rd*, 1951.]

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230. *Fatty Acids. Part I. 9-Hydroxyoctadec-12-enoic Acid,* a New Hydroxy-acid occurring in* Strophanthus sarmentosus *Seed Oil.*

By F. D. Gunstone

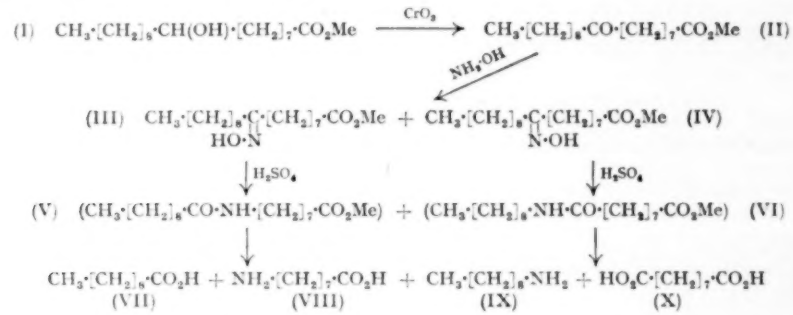
The unsaturated hydroxy-acid which forms 6·6% of the component acids of *Strophanthus sarmentosus* seed oil has been shown to be 9-hydroxyoctadec-12-enoic acid.

The steroid heart-poison aglycone, sarmentogenin, has been the subject of considerable study. It contains an oxygen atom at the 11-position and is therefore a potential starting point for the partial synthesis of cortisone (see Callow, Meikle, and Taylor, *Chem. and Ind.*, 1951, 336, who give earlier references). The oil present in the seeds, however, does not appear to have been examined although details for seed oils from other species of this genus have been reported (Matthes and Rath, *Arch. Pharm.*, 1914, **252**, 683; Tocco and Sanna, *Boll. Soc. ital. Biol. sper.*, 1935, **9**, 350; van Itallie, *Pharm. Weekbl.*, 1929, **66**, 677; Kühn, *Arch. Pharm.*, 1932, **270**, 395). Through the kindness of Dr. R. K. Callow of the Medical Research Council some of this seed oil has been made available. The results of its analysis by modern techniques are reported elsewhere (*J. Sci. Food Agric.*, in the press). Preliminary analysis disclosed an unusual acid. This remained with the more unsaturated acids which were soluble in acetone at −50°; its methyl ester distilled at a higher temperature than the C_{18} unsaturated esters; it behaved as though it were highly unsaturated (but see below), and was solid at room temperature and insoluble in light petroleum (b. p. 40—60°). These properties are those to be expected of an unsaturated hydroxy-acid and catalytic hydrogenation of a concentrate gave a saturated C_{18} hydroxy-acid. Subsequent oxidation

* Geneva numbering (CO_2H = 1).

gave the corresponding keto-acid. The best known acid of this type is ricinoleic acid (12-hydroxyoctadec-9-enoic acid) but the saturated hydroxy-acid obtained from *S. sarmentosus* seed oil was different from 12-hydroxystearic acid obtained from castor oil.

Concentrates of the unsaturated hydroxy-acid were obtained by a combination of low-temperature crystallisation and distillation. The acid has been shown to be 9-hydroxyoctadec-12-enoic acid by investigations which have revealed (*a*) the position of the hydroxyl group and (*b*) the position of the double bond.



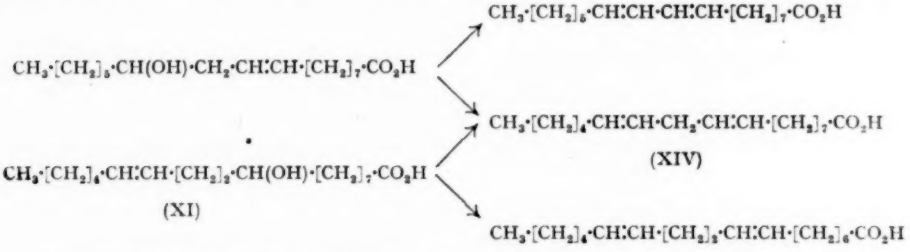
By the method first described by Baruch (*Ber.*, **1894**, **27**, 172) and subsequently used by Goldsobel (*Ber.*, 1894, **27**, 3121), Ross, Gebhart, and Gerecht (*J. Amer. Chem. Soc.*, **1949**, **71**, 283), and Riley (*J.*, 1951, 1346) a concentrate of the methyl ester of this new acid was reduced catalytically to methyl hydroxystearate (I), then oxidised to the corresponding keto-ester (II), and the mixed oximes (III and IV) from this were subjected to a Beckmann rearrangement and subsequent hydrolysis. Previous workers have hydrolysed the mixed amides with strong alkali under pressure but in this work it was conveniently effected by boiling 50% sulphuric acid. Of the four hydrolysis products three (VII, IX, and X) were isolated and two (VII and X) identified. The amine, unfortunately, decomposed before it could be identified. The monobasic and the dibasic acid were shown to be decanoic and azelaic acid respectively, indicating that the hydroxyl group was originally attached to the ninth carbon atom.

Despite the high iodine values obtained in the preliminary analysis the hydrogenation indicated that the acid contained only one ethylenic linkage. This was shown to be between the $C_{(12)}$ and $C_{(13)}$ by oxidation with potassium permanganate in acetone (Armstrong and Hilditch, *J. Soc. Chem. Ind.*, 1925, **44**, 43T). The monobasic acid (XII) was

identified as hexanoic acid. The dibasic acid fraction, after repeated crystallisation, gave a solid of empirical formula C_3H_5O. The equivalent showed that this solid was both a lactone and an acid and agreed well with the value $C_{12}H_{20}O_4$. The hydroxyl group has not been located but it should be in the γ-position and would consequently be expected to form a lactone very readily.

Long-chain hydroxy-acids are not common amongst the component acids of fats though they occur more frequently in waxes and are also known to be present in brain lipids. Ricinoleic acid is the best known acid of this type and occurs in *Ricinus* seed fats (*e.g.*, castor oil) and has also been reported in the seed fats of *Cephalocroton cordolfanus* (Henry and Grindley, *J. Soc. Chem. Ind.*, 1943, **62**, 60), *Agonandra brasiliensis* (Gurgel and de Amorim, *Mem. Inst. Chim. Rio de Janeiro*, 1929, **2**, 31), and from other unconfirmed sources. A hydroxy-acid present in *Vernonia anthelmintica* may be 11-hydroxyoctadec-9-enoic acid (Vidyarthi and Mallya, *J. Indian Chem. Soc.*, 1939, **16**, 479; Vidyarthi, *Patna Univ. J.*, 1945, **1**, 51; *Chem. Abstr.*, 1946, **40**, 4899), and Riley (*loc. cit.*) has recently shown that the

hydroxy-acid(s) present in *Onguekea Gore* (Engler) is a derivative of 8-hydroxystearic acid. Hydroxy-acids have also been claimed in other vegetable oils but these claims have been disproved. Both ricinoleic acid and our new hydroxy-acid could be dehydrated to give two diethenoid acids. It is perhaps significant that in both cases one product would be the widely distributed linoleic acid (XIV) and it may be that both hydroxy-acids represent precursors in the biogenesis of linoleic acid.



Oxidation with dilute alkaline potassium permanganate converts the acid into 9 : 12 : 13-trihydroxystearic acid. By following Kass and Radlove's procedure (*J. Amer. Chem. Soc.*, 1942, **64**, 2253) two forms of this acid have been isolated melting at 112—119° and 147·7—148·8°. The former, isolated in the smaller quantity, was not pure; a solid dibromide could not be isolated. The acid contains an asymmetric centre but attempts to determine whether it is optically active were inconclusive, the actual rotations measured being too small to be definite.

Throughout this work difficulty was encountered in determining the iodine value of fractions containing this hydroxy-acid. The values obtained were higher than expected and less concordant than usual and it appears that the hydroxyl group reacts with Wijs reagent. This does not occur with ricinoleic acid to any marked extent but Vidyarthi and Mallya (*loc. cit.*) reported the same difficulty with (?)11-hydroxyoctadec-9-enoic acid in which the hydroxyl group is adjacent to the double bond. They also claim that this difficulty does not occur when the hydroxyl group is acetylated and the author has confirmed that more satisfactory results are obtained with methyl 9-acetoxyoctadec-12-enoate. The effect with the hydroxy-acid is quite marked (see Experimental) but no explanation is offered for the different behaviour of 9-hydroxyoctadec-12-enoic and 12-hydroxyoctadec-9-enoic acid.

Experimental

Preparation of a Concentrate of the Unsaturated Hydroxy-acid.—The seed oil (600 g.) from *S. sarmentosus* was hydrolysed, the unsaponifiable portion (3·72 g.) was removed, and the resulting mixed acids (541·5 g.) were crystallised from acetone (5·4 l.) at −50°. The unsaturated hydroxy-acid remained in the soluble portion (209·3 g.). One concentrate was obtained by crystallising a portion (81 g.) of these acids from light petroleum (b. p. 40—60°; 10 ml. per g.) at −50° and by recrystallising the precipitated solids from the same solvent at −20°. The concentrate (*A*) (5·85 g.) so obtained was a viscous liquid slowly solidifying at room temperature. The remainder of the soluble acids, along with the material remaining in the mother-liquor from *A* (total, 198 g.), was methylated and distilled under reduced pressure, the fraction (*B*) (27·7 g.) boiling higher than the main fraction (unsaturated C_{18} esters) being retained. A portion of this material was acetylated (21 g.) and redistilled, the following fractions (*C*) being obtained [I.V. (Wijs) of methyl acetoxyoctadecenoate = 71·6]:

No.	C_1	C_2	C_3	C_4	C_5
Wt. (g.)	3·36	3·29	4·59	4·55	3·13
I.V.	132·6	96·2	81·9	76·2	73·3

A fourth concentrate (*D*) (1·89 g.)—possibly the purest—was obtained by hydrolysis of fraction C_5 and subsequent crystallisation of the acids from light petroleum (b. p. 40—60°; 10 ml. per g.) at −20°. This fraction was solid at room temperature and when subjected to alkali isomerisation (Hilditch, Morton, and Riley, *Analyst*, 1945, **70**, 67) gave no absorption band. A solution

in alcohol gave a value for $[\alpha]_D^{15}$ of $-0{\cdot}3°$ but the observed rotation (0·02°) was no greater than the variation in repeated determinations.

Determination of the Position of the Hydroxyl Group.—(a) *Hydrogenation of the unsaturated hydroxy-ester.* The concentrate *B* (7·4 g.) in ethanol (50 ml.) was hydrogenated in the presence of palladium–charcoal (uptake, 592 ml. at N.T.P. Calc. 530 ml.). After removal of the solvent, 7·5 g. of saturated esters were recovered.

(b) *Preparation of the mixed oximes* (III *and* IV). The hydroxystearate (I) in acetic acid (75 ml.) was oxidised by a 10% solution of chromium trioxide in acetic acid (32 ml.) at room temperature. After 30 minutes the solution was poured into water, excess of chromic acid reduced with sulphur dioxide, and the ketostearate (II) (7·2 g.) extracted with ether. Oximation was effected in boiling aqueous ethanol (130 ml.; 80%) with hydroxylamine hydrochloride (6 g.) and sodium acetate (9 g.) for 2 hours. After removal of some of the alcohol the mixed oximes (7·4 g.) were extracted with ether. They solidified at room temperature.

(c) *Beckmann rearrangement and hydrolysis of the mixed amides* (V *and* VI). The mixed oximes were heated in concentrated sulphuric acid (45 ml.) at 100° for 1 hour. The mixture was then diluted with water (80 ml.) to about 50% sulphuric acid and refluxed for 3 hours (slightly stronger acid or a longer reflux period would probably have given more satisfactory results). After further dilution the mixture was steam-distilled and the distillate (3 l.), extracted with ether, gave the monobasic acid fraction (VII) (0·70 g.). The distillation residue on extraction with ether yielded ether-soluble material separated into acidic (4·94 g.) and non-acidic (0·05 g.) portions. The aqueous residue was neutralised by potassium hydroxide and steam-distilled; the distillate (1 l.) gave the amine fraction (IX) (0·43 g.) on extraction; the distillation residue containing the amino-acid (VIII) was not further examined. The amine fraction decomposed (probably to the alkyl carbamate) before it could be examined.

(d) *Monobasic acid fraction* (VII). This fraction solidified at 0° and remained solid at room temperature. Distillation under reduced pressure gave fractions (*a*) 0·309 g., m. p. 26—29°, and (*b*) 0·096 g., m. p. 28—32° (lit., 31·3°), both of which gave rather high equivalent weights (203·1 and 185·1 respectively). The combined acids recovered from the equivalent-weight determination readily gave *p*-bromophenacyl decanoate, m. p. 64—65·5° (softens at 62°) (lit., 67·0°), undepressed when mixed with an authentic specimen (Found: C, 58·4; H, 6·6; Br, 21·8. Calc. for $C_{18}H_{25}O_3Br$: C, 58·5; H, 6·8; Br, 21·6%).

(e) *Dibasic acid fraction* (X). The non-volatile acidic component (4·94 g.) was extracted with boiling water (4 × 100 ml.). The insoluble portion (4·3 g.) was probably a mixture of unchanged amide and saturated acids. The combined aqueous extracts, when concentrated to *ca.* 20 ml. and cooled to 0°, yielded fairly pure azelaic acid (X) (0·50 g.), m. p. 103—106°, raised only to 104—106° (lit., 106°) when crystallised from water and from ethyl acetate and undepressed when mixed with an authentic specimen [Found: equiv., 94·8. Calc. for $C_7H_{14}(CO_2H)_2$: equiv., 94·1].

Determination of the Position of the Double Bond.—(a) *Oxidation of the unsaturated hydroxy-acid.* To the concentrate C_4 (4·4 g.) in boiling acetone (44 ml.) powdered potassium permanganate (17·6 g.) was added portionwise at such a rate as to maintain boiling. The solution was then refluxed for 4 hours, the acetone was removed, water and sulphuric acid (25%) were added, and the suspension was decolourised with sulphur dioxide and extracted with ether. The ethereal extract, after being washed with 10% aqueous potassium hydroxide and water, contained only unoxidised material (0·95 g.). The alkaline residue was heated, acidified, and steam-distilled. The distillate (2 l.) yielded the monobasic acid fraction (XII) (0·94 g.), and the residue gave the dibasic acid fraction (XIII) (1·93 g.) when extracted with ether.

(b) *Monobasic acid fraction* (XII). A portion (0·2 g.) of this fraction was converted very readily into its *p*-bromophenacyl ester, m. p. 69—70·5° (lit., 72·0°) undepressed when mixed with a sample prepared from authentic hexanoic acid (Found: C, 53·4; H, 5·4; Br, 25·4. Calc. for $C_{14}H_{17}O_3Br$: C, 53·7; H, 5·5; Br, 25·5%). Distillation under reduced pressure gave two fractions the equivalents of which (109·5 and 112·5) were slightly low.

(c) *Dibasic acid fraction* (XIII). The dibasic acid fraction was completely soluble in boiling water (200 ml.), and the solution, when concentrated to *ca.* 40 ml. and cooled to 0°, deposited a low-melting solid (0·90 g.). The m. p. after several crystallisations from aqueous methanol was raised to 66—67·5° (softens at 47°) (Found: C, 63·1; H, 8·9. $C_{12}H_{20}O_4$ requires C, 63·1; H, 8·8%). The compound behaves as a lactone and an acid giving two equivalents (228·8 and 114·1) by direct titration and by the procedure used for the equivalents of esters ($C_{12}H_{20}O_4$ requires 228·3 and 114·1): it is probably the lactone of 3-hydroxydecane-1 : 10-dicarboxylic acid.

Other Reactions of 9-*Hydroxyoctadec*-12-*enoic acid.*—(a) 9-*Hydroxy- and* 9-*keto-stearic acid.* Catalytic reduction of a concentrate of the unsaturated hydroxy-acid gave a product which after crystallisation from benzene melted at 81—82·5° (softened at 75°) (Tomecko and Adams, *J. Amer. Chem. Soc.*, 1927, **49**, 522, give m. p. 74—75° for the synthetic and therefore inactive 9-hydroxystearic acid) (Found: C, 71·8; H, 11·9. Calc. for $C_{18}H_{36}O_3$: C, 72·0; H, 12·1%). Reaction with methyl alcohol and anhydrous hydrogen chloride affords methyl 9-hydroxystearate, m. p. 50—53° (Tomecko and Adams, *loc. cit.*, give m. p. 45—46°) depressed to 45—51° when mixed with a sample of methyl 12-hydroxystearate (m. p. 57—59°) obtained from castor oil (Found: C, 72·6; H, 12·3. Calc. for $C_{19}H_{38}O_3$: C, 72·6; H, 12·2%). Oxidation (chromic oxide–acetic acid) of the hydroxy-acid gives 9-ketostearic acid, m. p. 79·5—81·0° (lit., 83°; Robinson and Robinson, *J.*, 1926, 2204; Behrend, *Ber.*, 1896, **29**, 807). An attempt to prepare methyl 9-acetoxystearate by reduction of the unsaturated ester (C_3) gave a compound crystallising from solution at 0° but melting below room temperature. Hydrolysis gave the same 9-hydroxystearic acid as that obtained above.

(b) 9 : 12 : 13-*Trihydroxystearic acid.* A concentrate (*A*) of the unsaturated hydroxy-acid (1·23 g.) was oxidised with alkaline potassium permanganate by Kass and Radlove's method (*loc. cit.*). The dried oxidation product was extracted with boiling light petroleum (b. p. 40—60°) (yielding 0·04 g.) and then with boiling chloroform (yielding 0·19 g.). After crystallisation from aqueous ethanol, aqueous acetic acid, and aqueous ethanol it melted at 112—119° (softened at 105°) and was probably an impure isomer of 9 : 12 : 13-trihydroxystearic acid (Found: C, 65·9; H, 10·6%). The chloroform-insoluble portion (0·61 g.) crystallised from ethanol, aqueous acetic acid, and finally ethanol and gave 9 : 12 : 13-*trihydroxystearic acid*, m. p. 147·7—148·8° (Found: C, 65·1; H, 11·0. $C_{18}H_{36}O_5$ requires C, 65·0; H, 10·9%).

(c) *Iodine value of* 9-*hydroxyoctadec*-12-*enoic acid.* The iodine value of a concentrate (*A*) of 9-hydroxyoctadec-12-enoic acid, which had not been distilled, was determined after 15, 30, 60, and 120 minutes, the liberated iodine being titrated *immediately* after addition of potassium iodide. Similar determinations were made on the mixed acids of castor oil, the results being:

Minutes	15	30	60	120
" Ricinoleic acid "	89·2	89·5	90·6	91·7
" 9-Hydroxyoctadec-12-enoic acid "	99·3	111·5	125·4	134·5

Methyl 9-acetoxyoctadec-12-enoate does not show this property. Of two similar (but not identical) concentrates of methyl 9-hydroxyoctadec-12-enoate one was acetylated. The iodine values (30 minutes) were 117·8 ± 0·6 and 72·9 ± 0·1 for the hydroxy- and acetoxy-esters respectively (Calc.: 81·2 and 71·6).

The author thanks Dr. R. K. Callow for supplying *S. sarmentosus* seed oil, Dr. J. P. Riley for the sample of methyl 12-hydroxystearate, and Mr. J. M. L. Cameron and Miss R. H. Kennaway for the microanalyses.

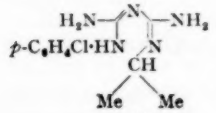
THE UNIVERSITY OF GLASGOW. [*Received, November* 30*th*, 1951.]

231. *Attempts to Prepare a Possible Metabolite of "Paludrine" (Proguanil) and Related* 1 : 3 : 5-*Triazines.*

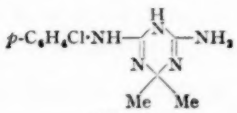
By Stanley Birtwell.

It is suggested that the metabolite of "Paludrine" (proguanil), which Hawking (*Nature*, 1947, **159**, 409) and others suggest is responsible for the antimalarial activity, may be an effective antagonist for folic acid. Proguanil itself is only a moderate folic acid antagonist (Falco *et al.*, *ibid.*, 1949, **164**, 107). If this is so, the metabolite may well be 4 : 6-diamino-1-*p*-chlorophenyl-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine. Attempts to prepare this and related triazines such as 4-amino-1-*p*-chlorophenyl-1 : 2-dihydro-2-imino-6-methyl-1 : 3 : 5-triazine, however, gave in all cases the inactive, isomeric compounds 4-amino-6-*p*-chloroanilino-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine and, *e.g.*, 2-amino-4-*p*-chloroanilino-6-methyl-1 : 3 : 5-triazine respectively, owing (in the latter case, and possibly in the former) to isomerisation of the 1-*p*-chlorophenyltriazines to the 6-*p*-chloroanilino-compounds.

There is much evidence to support the view that a metabolite, produced from the antimalarial drug "Paludrine" (proguanil) (I) in the animal body, is responsible for its plasmodicidal action (Hawking, *Nature*, 1947, **159**, 409, and later workers). Its constitution has previously been debated (Fraser and Kermack, *J.*, 1951, 2682) and *inactive* metabolites have been isolated, one of which is considered to be 2-amino-6-*p*-chloroanilino-1 : 4-dihydro-4 : 4-dimethyl-1 : 3 : 5-triazine (II) (Crounse, *J. Org. Chem.*, 1951, **16**, 492). In this connection, the present work on antimalarials containing the 1 : 3 : 5-triazine nucleus, and the underlying theory are of interest.



(I)



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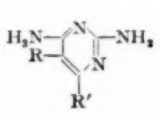
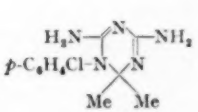


(III)



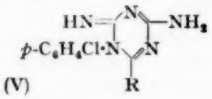
(IV)

Falco, Hitchings, Russell, and Vanderwerff (*Nature*, 1949, **164**, 107) have shown that proguanil (I) in common with many 2 : 4-diaminopyrimidines (III), is a folic acid antagonist with respect to *L. casei*. However, they observed that correlation between antifolic acid activity and antimalarial activity was obscure. A rational explanation of their results would follow if (*a*) the effective folic acid antagonist were the (animal) metabolite of proguanil and (*b*) *L. casei* were capable of metabolising the drug in this way only to a limited extent. Furthermore, since oxidation is a relatively common mode of detoxication, 4 : 6-diamino-1-*p*-chlorophenyl-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine (IV) is probably the metabolite in question. This compound also shows greater similarity to folic acid and the aminopyrimidines (III) than does proguanil (I).

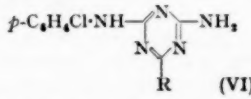
Owing to the difficulties in devising unambiguous routes to (IV) and the rather scanty evidence for the structure of (II) (Birtwell, Curd, Hendry, and Rose, *J.*, 1948, 1645; Crounse *loc. cit.*), which does not preclude many alternative structures, notably of the Schiff's base and four-membered ring types, syntheses of triazines of type (V) were first attempted.

When amidines react with dicyanimide (cf. Curd, Hendry, Kenny, Murray, and Rose, *J.*, 1948, 1630, for the reaction of amines with dicyanimide), the dicyanimide salt of the amidine is first formed, which on being heated alone or in a solvent rearranges to the 1 : 3 : 5-triazine. 2 : 4-Diamino-6-methyl- and 2 : 4-diamino-6-phenyl-1 : 3 : 5-triazine were prepared in this way from acetamidine and benzamidine respectively, and it appeared that the use of *N*-*p*-chlorophenylamidines in this reaction would afford an unambiguous route to 6-alkyl-4-amino-1-*p*-chlorophenyl-1 : 2-dihydro-2-imino-1 : 3 : 5-triazines (V). In fact,

N-*p*-chlorophenyl-acetamidine and -propionamidine gave the anilino-compounds 2-amino-4-*p*-chloroanilino-6-methyl- and -6-ethyl-1 : 3 : 5-triazine (VI; R = Me and R = Et respectively). *N*-*p*-Chlorophenyl-*N'*-cyanoguanidine was isolated as a by-product, but does not appear to be involved in the formation of the anilino-triazine (VI): it does not

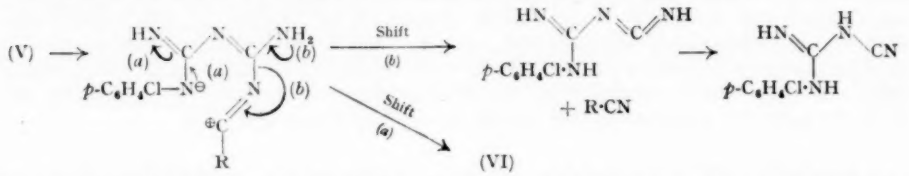


(V)



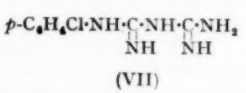
(VI)

combine with methyl or ethyl cyanide under the conditions applying in the above reaction, and yields only a trace of (VI; R = Et) when similarly treated with *N*-*p*-chlorophenyl-propionamidine. The known processes for the preparation of triazines from cyanoguanidines and nitriles or amidines involve much higher temperatures and pressures and usually an alkaline catalyst (*e.g.*, Ostrogovich, *Chem. Abs.*, 1911, 2099; U.S.P. 2 302 162; B.P. 583 720). Therefore, in the reaction between substituted amidines and dicyanimide, compounds of type (V) are first formed but, being unstable at the temperature of the reaction, undergo fission of the $N_{(1)}$–$C_{(6)}$ bond, subsequently cyclising on the free amino-group to give the more stable, aromatic structures (VI). It is believed that fission of the $N_{(1)}$–$C_{(6)}$ bond is also a necessary preliminary for the formation of the by-products *N*-*p*-chlorophenyl-*N'*-cyanoguanidine and alkyl cyanide (not isolated), the mechanism of decomposition and isomerisation of the unstable dihydrotriazines (V) being:

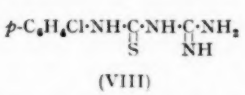


Compounds (VI; R = Me and Et) had no plasmodicidal activity when tested against *P. gallinaceum* in chicks.

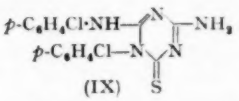
Attempts to prepare the dihydrotriazine (IV) by methods which, it was recognised, might lead only to isomers or mixtures of isomers, were then made. Three main routes, commencing respectively from proguanil (I), *p*-chlorophenyldiguanide (VII), and *N*-amidino-N'-*p*-chlorophenylthiourea (VIII), have been explored.



(VII)



(VIII)



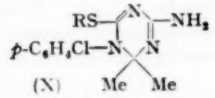
(IX)

Oxidation of (I) by acid or alkaline permanganate, lead tetra-acetate, hydrogen peroxide, or potassium ferricyanide gave no recognisable products.

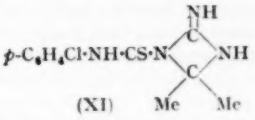
Acetone and (VII) under reflux in acetic acid gave the triazine (II); the hydrochloride of (VII) failed to condense with acetone although the related but much less basic dithiobiurets condense readily, in the presence of strong acid, to give keturets (Fromm, *Annalen*, 1893, **275**, 30). Acetone diethyl acetal and (VII) at 130° gave a complex mixture from which two substances were isolated with difficulty. Analytical data in neither case corresponded to (IV) and identification was not completed.

The method of Slotta, Tschesche, and Dressler (*Ber.*, 1930, **63**, 208) was used for the preparation of (VIII) from *p*-chlorophenyl *iso*thiocyanate and guanidine. A compound $C_{15}H_{11}N_5SCl_2$ was also isolated which, it is believed, is (IX) (cf. Crowther, Curd, Richardson, and Rose, *J.*, 1948, 1636, who isolated similar compounds from the reaction of *p*-chlorophenyl *iso*thiocyanate with alkylguanidines). Acetone reacted readily with (VIII) in the presence of piperidine: the yield of condensation product varied with the amount of catalyst used, being a maximum (85%) with 50 c.c. of piperidine per mole of (VIII). The same product was obtained in poor yield when the reaction was catalysed by hydrochloric

acid. It has been assigned structure (X; R = H) in view of its alkali solubility, its retention of sulphur in the presence of reagents such as ammoniacal silver nitrate, mercuric oxide, etc., its ready *S*-alkylation, and in particular the reaction with chloroacetic acid which does not give a cyclic structure as is the case with substituted thioureas containing two replaceable hydrogen atoms (Johnson, Pfau, and Hodge, *J. Amer. Chem. Soc.*, 1912, **34**, 1041). Although alkali solubility is doubtful it is possible that structure (XI) would also possess these properties, but it might be expected to give the same colour reaction with ammoniacal nickel salts as an amidinothiourea. Our compound does not do so, and as subsequent stages of the synthesis failed to give the



(X)



(XI)

desired (IV), more rigorous proof has not been sought. Replacement of the ethylthio-group of (X; R = Et) by amino has been tried under a variety of conditions, *viz.*, boiling the hydriodide with alcoholic ammonia, heating the hydriodide or the free base with methanolic ammonia in sealed tubes at 55—60°, and fusion of the hydriodide with ammonium acetate. In all cases, the anilino-triazine considered to be (II) was isolated, accompanied by decomposition products such as guanidine, *p*-chlorophenylguanidine, and, in the ammonium acetate fusion, *p*-chloroacetanilide, as well as a number of compounds which have been identified only as far as their empirical formulæ. A clear explanation of these results cannot be given. It may be that (IV) and not (II) is the correct formula for the reaction product of *p*-chlorophenyldiguanide and acetone in the presence of piperidine. Alternatively, (II) may be formed by reaction of ammonia with intermediates arising by decomposition of (X), or more probably as a result of a rearrangement such as has been suggested for the conversion of the unstable (V) into (VI).

Other reactions which have been tried in order to obtain the desired type of compound include the condensation of N^1-diethylaminoethyl-N^2-phenyldiguanide with acetone, and reaction of benzoyl-*p*-chlorophenylcyanamide with guanidine. The materials isolated appear to be hydrolysis products of the desired compounds—as determined from analytical data—6-diethylaminoethylamino(or 1-diethylaminoethyl)-1 : 2-dihydro-4-hydroxy-2 : 2-dimethyl-1-phenyl(or 6-anilino)-1 : 3 : 5-triazine in the former, and 1-*p*-chlorophenyl-1 : 2-dihydro-4-hydroxy-2-keto-6-phenyl-1 : 3 : 5-triazine in the latter case.

[Note added in proof.] Carrington, Crowther, Davey, Levi, and Rose recently reported (*Nature*, 1951, **168**, 1080) the isolation of a metabolite having ten times the activity of the parent drug. Its structure (IV), predicted by us on theoretical grounds, has been confirmed by *X*-ray analysis. Ready conversion of the metabolite into the inactive isomer (II), by the action of heat or alkali, confirms our suspicion that the failure to obtain (IV) by the methods adopted was, in fact, due to such an isomerisation. The synthesis of (IV) from *N'*-*p*-chlorophenyldiguanide and acetone has been accomplished (*loc. cit.*), under unspecified conditions.

Experimental

M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss of Oxford.

N-p-*Chlorophenylacetamidine*.—An ethereal solution of methylmagnesium iodide (120 c.c., 0·25 mole) was added during 5 minutes to a stirred solution of *p*-chlorophenylcyanamide (15·2 g., 0·1 mole) in anisole (100 c.c.). Methane was evolved and ether distilled. The mixture was heated to 90—100°, more ether being distilled off, and this temperature was maintained for 2½ hours. After cooling, the whole was poured into dilute hydrochloric acid and ice. The aqueous layer was separated and basified with sodium hydroxide solution (addition of ice), and the precipitate filtered off (gravity). The filtrate and the filter paste were extracted with chloroform (300 c.c.). The extract, after being dried (Na_2SO_4), was evaporated to small bulk, *N*-*p*-chlorophenylacetamidine crystallising. Last traces of solvent were removed on a porous tile, and the product was obtained as pale brown prisms (12·6 g.), m. p. 112—115° (Gage, *J.*, 1949, 221, gives m. p. 116—117° after crystallisation from *cyclo*hexane).

Reaction of Dicyanimide with Amidines.—(a) *Benzamidine.* Benzamidine hydrochloride (1·6 g.) was added to sodium dicyanimide (0·9 g.) in water (20 c.c.). The *dicyanimide* salt of benzamidine, which crystallised, was collected and dried *in vacuo* ($CaCl_2$) (1·0 g.; m. p. 154°). When it was heated to 160° in an oil-bath, a vigorous reaction set in and the temperature rose spontaneously to 250°. After it had subsided, the temperature was kept at 150—160° for 10 minutes. The product was cooled and digested with 2N-hydrochloric acid (20 c.c.) at 60°, and the filtered extract poured into excess of dilute sodium hydroxide solution (ice), 2 : 4-diamino-6-phenyl-1 : 3 : 5-triazine being precipitated (0·7 g.; m. p. 221—225°). After crystallisation from alcohol it had m. p. 223—225° (Found: C, 57·4; H, 5·1; N, 37·2. Calc. for $C_9H_9N_5$: C, 57·7; H, 4·8; N, 37·4%).

(b) *Acetamidine.* Acetamidine hydrochloride (9·4 g.) and sodium dicyanimide (9·0 g.) were stirred in absolute alcohol (100 c.c.) and heated under reflux for 1 hour. After cooling, the sodium chloride was filtered off, and the filtrate evaporated to dryness *in vacuo*. A crystalline residue of the dicyanimide salt of acetamidine (12·5 g.) remained, m. p. 94° after drying at 80—90°.

A portion (5·0 g.) was stirred in dry benzene (75 c.c.), and traces of alcohol and water were removed as azeotropes by distillation of about two-thirds of the solution. Nitrobenzene (25 c.c.) was added and the mixture heated to the b. p. for about 5 minutes, with the apparatus set for distillation. Much ammonia was evolved. The suspension was then filtered, and the solid washed with benzene, dried, and dissolved in water (50 c.c.) containing 2N-sodium hydroxide (5 c.c.) at 60°. Some insoluble material was removed, and the concentration of sodium hydroxide in the filtrate increased to about 10% by addition of a concentrated solution of the alkali. Crystalline 2 : 4-diamino-6-methyl-1 : 3 : 5-triazine, giving the characteristic blue colour with iodine–potassium iodide solution, was precipitated. It was collected, washed with a small amount of 2N-sodium hydroxide, then with alcohol, and finally crystallised from alcohol, whereafter it had m. p. 270—272° (Found: C, 38·25; H, 5·7. Calc. for $C_4H_7N_5$: C, 38·4; H, 5·6%).

(c) N-p-*Chlorophenylacetamidine.* 2N-Hydrochloric acid (30 c.c.) was added to a suspension of the amidine (10·5 g.) in water (50 c.c.) until an acid reaction to Congo-red was obtained. The solution was clarified and treated with sodium dicyanimide (5·5 g.) in water (30 c.c.). Scratching caused separation of the *dicyanimide* salt of *N*-*p*-chlorophenylacetamidine which was filtered off, washed with water, and dried on a porous title *in vacuo* over phosphoric oxide (11·3 g.; m. p. 144—146°). A sample, recrystallised from water at 70—80°, was obtained as small, almost colourless, needles, m. p. 145—146° (Found: C, 50·75; H, 4·25; N, 29·4. $C_{10}H_{10}N_5Cl$ requires C, 51·0; H, 4·25; N, 29·7%). A portion of this salt (7·0 g.) in dry butanol (K_2CO_3) (35 c.c.) was heated under reflux for 2 hours. The butanol was distilled in steam, and the residual hot suspension acidified (hydrochloric acid) and cooled. A crystalline precipitate (1·3 g.; m. p. 189—200°) which separated was filtered off and washed with water to a total volume of filtrate of 90—100 c.c. After purification through dilute sodium hydroxide solution, and three crystallisations from 33% alcohol, it had m. p. 208°, undepressed on admixture with *N*-*p*-chlorophenyl-*N'*-cyanoguanidine (Found: C, 49·35; H, 3·7; N, 29·0; Cl, 18·0. Calc. for $C_8H_7N_4Cl$: C, 49·4; H, 3·6; N, 28·8; Cl, 18·3%). The aqueous, acid filtrate was clarified after being warmed to 25—30°, and treated with concentrated nitric acid (14 c.c.) with good stirring. The crystalline nitrate which separated was collected, washed with dilute nitric acid, dissolved in hot water (50 c.c.), and poured into excess of sodium hydroxide solution and ice. The precipitate of 2-amino-4-*p*-chloroanilino-6-methyl-1 : 3 : 5-triazine (VI; R = Me) was dried and crystallised from chlorobenzene; it was obtained as almost colourless prisms (2·6 g.; m. p. 198—199°) (Curd, Landquist, and Rose, *J.*, 1947, 154, give m. p. 195—196°) (Found: C, 51·3; H, 4·4; N, 30·0. Calc. for $C_{10}H_{10}N_5Cl$: C, 51·0; H, 4·25; N, 29·7%).

(d) N-p-*Chlorophenylpropionamidine.* The *dicyanimide* salt (4·0 g.; m. p. 120—122°), prepared as in (c) from *p*-chlorophenylpropionamidine (Birtwell, *J.*, 1949, 2561) (4·8 g.), sodium dicyanimide (2·5 g.), and 2N-hydrochloric acid (12·5 c.c.), crystallised from water in almost colourless prisms, m. p. 121—122° (Found: C, 53·0; H, 4·9; N, 28·2. $C_{11}H_{12}N_5Cl$ requires C, 52·9; H, 4·8; N, 28·1%). A portion of the salt (3·5 g.) was heated under reflux in dry butanol (K_2CO_3) for 2 hours. The butanol was distilled off in steam and the residual solution acidified with hydrochloric acid. Insoluble material was filtered off, washed with water (total filtrate volume, 50 c.c.) and extracted with water (50 c.c.) at 50—60°. The filtered extract was poured into excess of sodium hydroxide solution and ice, 2-amino-4-*p*-chloroanilino-6-ethyl-1 : 3 : 5-triazine (VI; R = Et) (1·4 g.; m. p. 171—172°) separating. A further amount (0·35 g.; m. p. 169—170°) was obtained by addition of nitric acid to the filtrate from the steam-distillation

as in (c). The combined crops, after crystallisation from toluene, had m. p. 174—175°, undepressed on admixture with an authentic specimen (Birtwell, *loc. cit.*) (Found: C, 53·1; H, 5·0; Cl, 14·0. Calc. for $C_{11}H_{12}N_5Cl$: C, 52·9; H, 4·8; Cl, 14·2%).

Attempted Reaction of N-p-*Chlorophenyl*-N′-*cyanoguanidine with Ethyl Cyanide.*—A mixture of *N*-*p*-chlorophenyl-*N*′-cyanoguanidine (2·0 g.), ethyl cyanide (1·0 c.c.), and butanol (15 c.c.) was heated under reflux for 3 hours. Unchanged *N*-*p*-chlorophenyl-*N*′-cyanoguanidine (1·65 g.; m. p. 210—211°) crystallised on cooling. No basic material was obtained by dilution of the filtrate with benzene and extraction with hydrochloric acid.

The course of the reaction was unaffected by the addition of acid (HCl, NH_4Cl) or basic (NaOEt) catalysts, or by slight modifications in the experimental procedure.

Reaction of N-p-*Chlorophenyl*-N′-*cyanoguanidine with* N-p-*Chlorophenylpropionamidine.*—*N*-*p*-Chlorophenyl-*N*′-cyanoguanidine (1·4 g.) and *N*-*p* chlorophenylpropionamidine (1·3 g.) were heated under reflux for 3 hours in butanol (10 c.c.) containing a trace of hydrochloric acid. Unchanged *N*-*p*-chlorophenyl-*N*′-cyanoguanidine (1·0 g.; m. p. 210—212°) which crystallised on cooling was filtered off, and the filtrate was distilled in steam. The residue was acidified with hydrochloric acid, and filtered at the boil. The filtrate, on cooling, deposited crystals which were collected, dissolved in hot water, and poured into sodium hydroxide solution, 2-amino-4-*p*-chloroanilino-6-ethyl-1 : 3 : 5-triazine (VI; R = Et) (0·1 g.; m. p. 171—172°) being obtained.

Preparation of 2-*Amino*-6-p-*chlorophenyl*-1 : 4-*dihydro*-4 : 4-*dimethyl*-1 : 3 : 5-*triazine* (II) *in Acetic Acid Solution* (cf. Birtwell, Curd, Hendry, and Rose, *J.*, 1948, 1645).—*p*-Chlorophenyldiguanide (VII) (10·5 g.), acetone (10 c.c.), and glacial acetic acid (10 c.c.) were mixed, whereupon the acetate crystallised. The suspension was heated under reflux for 40 hours until almost homogeneous, and, after cooling, was poured into sodium hydroxide solution and ice, an oil being precipitated. The addition of benzene caused the mixture to separate into two layers with 2-amino-6-*p*-chlorophenyl-1 : 4-dihydro-4 : 4-dimethyl-1 : 3 : 5-triazine (II) at the interphase. This was collected and crystallised from aqueous alcohol, the hydrate of the base (1·0 g.) being obtained m. p. 135—136° (Birtwell *et al.*, *loc. cit.*, give m. p. 130—131°).

Reaction of p-*Chlorophenyldiguanide* (VII) *with Acetone Diethyl Acetal.*—A paste of *p*-chlorophenyldiguanide (VII) (10·5 g.) in acetone diethyl acetal (10·0 g.) was heated under reflux ($CaCl_2$ tube) in an oil-bath at 120°, so that the acetal was boiling gently. After 18 hours, benzene (100 c.c.) was added, and moist carbon dioxide was passed through the cooled, filtered solution. The precipitated carbonates, on treatment with cold, dilute hydrochloric acid gave an insoluble *hydrochloride*, which after two crystallisations from butanol had m. p. 288—289° (Found: C, 40·7; H, 4·0; N, 29·5; Cl, 24·8. $C_{10}H_{11}N_6Cl,HCl$ requires C, 41·8; H, 4·2; N, 29·3; Cl, 24·8%). The benzene filtrate from the carbonates was treated with dry hydrogen chloride. The precipitated hydrochlorides, suspended in warm alcohol, and treated with sodium hydroxide solution, gave a crude *base* on dilution with water. After three crystallisations from aqueous dioxan it had m. p. 203—205° (Found: C, 53·0; H, 5·1; N, 19·1; Cl, 16·0. $C_{10}H_{12}ON_3Cl$ requires C, 53·2; H, 5·3; N, 18·6; Cl, 15·7%).

N-*Amidino*-N′-p-*chlorophenylthiourea* (VIII).—Guanidine hydrochloride (29·0 g.) and a solution of sodium (6·0 g.) in acetone (200 c.c.) were stirred at room temperature for 1 hour. *p*-Chlorophenyl *iso*thiocyanate was added gradually with cooling, and after 24 hours' stirring the mixture was heated under reflux for 1 hour, then cooled and filtered. When the filtrate was poured into water an oil separated, which became slowly semi-solid. The water was decanted and the residue treated with a small amount of alcohol, giving a solid, m. p. 189° (decomp.) (19·0 g.). After being dried for a short time at 100°, it was boiled with methanol (*ca.* 300 c.c.), and the insoluble 4-*amino*-6-p-*chloroanilino*-1-p-*chlorophenyl*-1 : 2-*dihydro*-2-*thio*-1 : 3 : 5-*triazine* (IX) filtered off; it had m. p. 290° (decomp.) after two crystallisations from 2-ethoxyethanol (Found: C, 49·5; H, 3·3; N, 19·0. $C_{15}H_{11}N_5SCl_2$ requires C, 49·5; H, 3·0; N, 19·2%). The methanol filtrate on cooling gave N-*amidino*-N′-p-*chlorophenylthiourea* (VIII), m. p. 191° (decomp.) (10·3 g.) (Found: C, 42·2; H, 3·6; N, 24·5. $C_8H_9N_4SCl$ requires C, 42·0; H, 3·9; N, 24·5%). A further small amount was obtained by evaporation of the filtrate.

4-*Amino*-1 : 2-*dihydro*-6-*mercapto*-2 : 2-*dimethyl*-1-*phenyl*-1 : 3 : 5-*triazine.*—*N*-Amidino-*N*′-phenylthiourea (Slotta *et al.*, *Ber.*, 1930, **63**, 208) (2·3 g.), acetone (15 c.c.), and piperidine (0·1 c.c.) were heated under reflux for 20 hours. Complete solution was not obtained. After cooling, the insoluble material was filtered off and recrystallised from butanol, to give the *mercaptotriazine*, m. p. 240° (decomp.) (Found: C, 56·3; H, 5·9; N, 23·9; S, 13·4 $C_{11}H_{14}N_4S$ requires C, 56·4; H, 6·0; N, 23·9; S, 13·7%).

4-*Amino*-1-p-*chlorophenyl*-1 : 2-*dihydro*-6-*mercapto*-2 : 2-*dimethyl*-1 : 3 : 5-*triazine* (X; R =

H).—*N*-Amidino-N′-*p*-chlorophenylthiourea (VIII) (34·3 g.), acetone (300 c.c.), and piperidine (7·5 c.c.) were heated under reflux with stirring for 3 hours. The insoluble *mercaptotriazine* was collected, washed with acetone, and dried at 100°; it (34·0 g.) had m. p. 229° (decomp.), unchanged on recrystallisation from butanol (Found: N, 21·4; S, 12·3. $C_{11}H_{13}N_4SCl$ requires N, 20·9; S, 11·9%).

4-*Amino*-1-p-*chlorophenyl*-1 : 2-*dihydro*-2 : 2-*dimethyl*-6-*methylthio*-1 : 3 : 5-*triazine* (X; R = Me).—The triazine (X; R = H) (1·3 g.), dimethyl sulphate (1·0 c.c.), and 2N-sodium hydroxide solution were shaken together for 3 hours, then warmed on the steam-bath for 15 minutes. The product was filtered off after cooling, washed with water, stirred with ether, and collected on a porous tile. It was taken up in acetone, filtered from insoluble material, and evaporated to dryness. The residue, recrystallised twice from *cyclo*hexane–benzene (3 : 1), gave the required *base* (X; R = Me), m. p. 171° (Found: C, 50·9; H, 5·6; N, 19·2. $C_{12}H_{15}N_4SCl$ requires C, 51·0; H, 5·3; N, 19·8%)

4-*Amino*-1-p-*chlorophenyl*-6-*ethylthio*-1 : 2-*dihydro*-2 : 2-*dimethyl*-1 : 3 : 5-*triazine* (X; R = Et).—(*a*) The mercapto-triazine (X; R = H) (4·0 g.), ethyl iodide (4·0 c.c.), and absolute alcohol (40 c.c.) were heated under reflux for 30 minutes, a homogeneous solution being obtained. The bulk of the solvent was evaporated off, and benzene (75 c.c.) added. Distillation of a further 20—25 c.c. removed the remaining alcohol, and the solution when cooled and scratched gave 4-*amino*-1-p-*chlorophenyl*-6-*ethylthio*-1 : 2-*dihydro*-2 : 2-*dimethyl*-1 : 3 : 5-*triazine hydriodide* (5·6 g.; m. p. 181—182°). After crystallisation from water it had m. p. 182—183° (Found: C, 37·3; H, 4·4. $C_{13}H_{17}N_4SCl$ requires C, 36·8; H, 4·2%). A portion of the hydriodide, dissolved in hot water and poured into dilute sodium hydroxide solution and ice, gave the *base* (X; R = Et), which was dried *in vacuo* over sulphuric acid, then crystallised twice from *cyclo*hexane; it had m. p. 173—174° (Found: C, 52·9; H, 5·9; N, 18·3; S, 10·6. $C_{13}H_{17}N_4SCl$ requires C, 52·6; H, 5·7; N, 18·9; S, 10·8%). The picrate had m. p. 191—193°.

(*b*) *N*-Amidino-*N*′-*p*-chlorophenylthiourea (11·4 g.), 10N-hydrochloric acid (6·0 c.c.), and acetone (50 c.c.) were heated under reflux for 20 hours, then cooled, and insoluble material filtered off. The filtrate was poured into excess of 2N-sodium hydroxide solution, and the supernatant liquid decanted from the resulting oily precipitate. On acidification of the solution, and then basification with ammonia, a precipitate of crude (X; R = H) (3·2 g.) was obtained. After drying, it was converted into 4-amino-1-*p*-chlorophenyl-6-ethylthio-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine hydriodide as in (*a*) above, which after recrystallisation from chlorobenzene had m. p. 180—182° and gave a picrate, m. p. 191—193°, identical with the picrate obtained in (*a*).

4-*Amino*-6-*carboxymethylthio*-1-p-*chlorophenyl*-1 : 2-*dihydro*-2 : 2-*dimethyl*-1 : 3 : 5-*triazine* (X; R = $CH_2{\cdot}CO_2H$).—The mercapto-triazine (X; R = H) (1·0 g.), chloroacetic acid (1·0 g.), and water (10 c.c.) were boiled under reflux. At no time was a homogeneous solution obtained. The reaction mixture was cooled, and the insoluble material filtered off [0·15 g.; m. p. 241° (decomp.)]. The filtrate was basified with sodium hydroxide solution, and a stream of carbon dioxide passed through the solution, giving a further quantity of the same product [0·75 g.; m. p. 222° (decomp.)]. This substance was soluble in acids and alkalis but insoluble in all the usual solvents. It was converted into the *picrate* of 4-amino-6-carboxymethylthio-1-*p*-chlorophenyl-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine by boiling it with aqueous-alcoholic picric acid, and after recrystallisation from 66% alcohol this had m. p. 153—155° (decomp.) (0·5 g.) (Found: C, 41·5; H, 3·6; S, 5·7. $C_{13}H_{15}O_2N_4SCl,C_6H_3O_7N_3$ requires C, 41·0; H, 3·2; S, 5·7%).

Reactions of the Hydriodide of 4-*Amino*-1-p-*chlorophenyl*-6-*ethylthio*-1 : 2-*dihydro*-2 : 2-*dimethyl*-1 : 3 : 5-*triazine* (X; R = Et).—(a) *With ammoniacal methanol solution.* The hydriodide (6·0 g.) of (X; R = Et) in a saturated solution of ammonia in methanol (40 c.c.) was heated in a sealed tube at 55—60° for 6 hours. After cooling, the solution was filtered and evaporated to dryness. The residue was separated from a small amount of oil by dissolution in dilute hydrochloric acid. Mineral acidity was removed by sodium acetate, then a solution of picric acid in aqueous sodium acetate was added. The bulky picrate was collected and washed with warm water (A) (3·0 g.; m. p. 200—220°). The mother-liquors on being kept overnight gave a further picrate (B) [0·2 g.; m. p. 310° (decomp.)]. Product (A) was treated with a small amount of boiling ethyl acetate, then cooled, and the insoluble material filtered off. After several recrystallisations from alcohol, the picrate of 2-amino-6-*p*-chloroanilino-1 : 4-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine, m. p. and mixed m. p. 239—240°, was obtained. The ethyl acetate mother-liquors were evaporated to dryness, and the residue recrystallised from glacial acetic acid, then from aqueous alcohol, giving *p*-chlorophenylguanidine picrate, m. p. 230°, not

depressed on admixture with an authentic specimen. Product (B) was recrystallised from glacial acetic acid to give guanidine picrate, m. p. 320° (decomp.).

(b) *With ammonium acetate.* Ammonium acetate (4·0 g.) was fused at 160° and the hydriodide (1·0 g.) of (XI; R = Et) added. The temperature was kept at 160—180° for 1 hour. The reaction mixture was cooled and diluted with water, *p*-chloroacetanilide crystallising (0·1 g.; m. p. 177—179°). Aqueous picric acid was added to the boiling filtrate, and the solution allowed to cool overnight; a picrate (0·85 g.) crystallised. It was extracted with a small amount of acetone, and the insoluble (0·15 g.) material crystallised from a large volume of acetone, giving guanidine picrate, m. p. and mixed m. p. 325° (decomp.) (Found: C, 29·7; H, 2·8; N, 29·2. Calc. for $CH_5N_3,C_6H_3O_7N_3$: C, 29·2; H, 2·8; N, 29·2%). The acetone extract was evaporated to dryness and re-extracted with boiling water (50 c.c.). The insoluble material was filtered off, recrystallised from alcohol, and extracted with a small amount of ethyl acetate, leaving 2-amino-6-*p*-chloroanilino-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine picrate, m. p. and mixed m. p. 238—239°. The aqueous extract, on cooling, deposited crystals of *p*-chlorophenylguanidine picrate, which after successive crystallisations from water and ethyl acetate had m. p. 235° (Found: C, 39·1; H, 2·3; N, 21·0; Cl, 9·6. Calc. for $C_7H_8N_3Cl,C_6H_3O_7N_3$: C, 39·2; H, 2·3; N, 21·0; Cl, 8·9%).

Reaction of 4-*Amino*-1-p-*chlorophenyl*-6-*ethylthio*-1 : 2-*dihydro*-2 : 2-*dimethyl*-1 : 3 : 5-*triazine* (X; R = Et) *with Ammonia.*—The triazine (X; R = Et) (4·0 g.), dissolved in a saturated solution of ammonia in methanol (40 c.c.), was heated in a sealed tube at 55—60° for 6 hours. The reaction mixture was evaporated to dryness after clarification, and the tarry residue extracted with tepid benzene, leaving a small amount of sparingly soluble, semi-solid material (A). Carbon dioxide was passed through the solution, and the precipitated carbonate (B) collected and boiled with benzene; some carbon dioxide was then evolved and a portion of the material dissolved. The insoluble material (C) was filtered off, and carbon dioxide was passed through the cold filtrate. The precipitated carbonate (D) (hygroscopic) was filtered off and dried *in vacuo*. Hydrogen chloride was passed through the main benzene filtrate (from B), and the hydrochloride which separated was filtered off. It was extracted with acetone, with decantation from a small amount of oil, and the residue, after evaporation of the acetone, was dissolved in water. Addition of a sodium acetate–picrate acid solution gave the picrate (E). Product (A), treated with alcoholic picric acid gave 2-amino-6-*p*-chloroanilino-1 : 4-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine picrate, m. p. and mixed m. p. 239—240° after two recrystallisations from alcohol. A further quantity of this compound was obtained by warming the carbonate (C) with aqueous picric acid and recrystallising the salt several times from alcohol. The material (D), treated with aqueous-alcoholic picric acid, gave a *picrate* which, after several crystallisations from glacial acetic acid, had m. p. 197—198°. It has not been identified (Found: C, 36·7; H, 2·5; N, 22·0; Cl, 5·5. $C_9H_9N_4Cl,2C_6H_3O_7N_3$ requires C, 36·7; H, 2·3; N, 21·4; C, 5·4%). Picrate (E) was extracted with cold acetone, and the residue recrystallised several times from glacial acetic acid, to give an unidentified *picrate*, m. p. 257° (Found: C, 38·0; H, 2·5; N, 21·8; Cl, 9·2%). The acetone extract was evaporated to dryness and the product crystallised twice from absolute alcohol, to give the picrate, m. p. and mixed m. p. 192—193°, of the starting material (X; R = Et).

Reaction of Guanidine and Benzoyl-p-*chlorophenylcyanamide.*—Guanidine hydrochloride (0·95 g.), sodium methoxide (0·54 g.), and benzoyl-*p*-chlorophenylcyanamide (3·5 g.) were heated under reflux in butanol (20 c.c.) for 2 hours. After cooling, the product, mixed with sodium chloride, was filtered off, washed with butanol, and dried at 100°. Sodium chloride was extracted with water, and the residue (0·6 g.; m. p. 235—238°) recrystallised from glacial acetic acid, to give 1-*p*-chlorophenyl-1 : 2-dihydro-4-hydroxy-2-keto-6-phenyl-1 : 3 : 5-triazine (Found: C, 60·2; H, 3·9; N, 14·2. $C_{15}H_{10}O_2N_3Cl$ requires C, 60·1; H, 3·4; N, 14·0%).

N^1-2′-*Diethylaminoethyl*-N^2-*phenyldiguanide and a Hydroxy-triazine.*—*N*-Amidino-*N*′-phenylthiourea (Slotta *et al.*, *loc. cit.*) and diethylaminoethylamine (5·0 g.) in absolute alcohol (50 c.c.) were stirred and heated under reflux for 5 hours with mercuric oxide (12·0 g.). The mixture was cooled, mercury salts were filtered off, and the amber-coloured filtrate was evaporated to dryness under diminished pressure (bath-temp. ≯90°). The residue was taken up in 2N-hydrochloric acid, clarified, and made alkaline with ammonia. The precipitate was filtered off and discarded. The filtrate gave a yellow oil on basification (sodium hydroxide solution), which was extracted into ether and dried (KOH). A yellow, gummy residue remained on evaporation of the solvent. Without further purification it was heated in acetone (25 c.c.) for 24 hours, then cooled, and carbon dioxide was passed through the solution. A carbonate was obtained (0·9 g.; m. p. 98—99° after shrinking), which dissolved in boiling acetone with evolution of

carbon dioxide. On retreatment of the cooled solution with carbon dioxide, the carbonate of N^1-2′-*diethylaminoethyl*-N^2-*phenyldiguanide* crystallised (m. p. 98—100° after shrinking) (Found: C, 53·0; H, 8·1; N, 24·2. $C_{14}H_{24}N_6,H_2CO_3,\frac{1}{2}H_2O$ requires C, 53·3; H, 7·6; N, 24·8%). The *picrate* separated from alcohol in yellow prisms, m. p. 186—187° (Found: C, 41·9; H, 4·0; N, 22·6. $C_{14}H_{24}N_6,2C_6H_3O_7N_3,H_2O$ requires C, 42·5; H, 4·1; N, 22·9%). The main acetone filtrate was evaporated to dryness and converted into the picrate by treament with alcoholic picric acid. After several recrystallisations from acetone–alcohol 6-*diethylaminoethylamino*-(or 1-*diethylaminoethyl*)-1 : 2-*dihydro*-4-*hydroxy*-2 : 2-*dimethyl*-1-*phenyl*-(or 6-*anilino*)-1 : 3 : 5-*triazine picrate* crystallised; it had m. p. 196—198° (Found: C, 43·9; H, 4·5; N, 18·9. $C_{17}H_{27}ON_5,2C_6H_3O_7N_3,H_2O$ requires C, 43·8; H, 4·4; N, 19·4%).

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232. o-*Mercapto-azo-compounds. Part II.** 1-(1-*Mercapto*-2-*naphthylazo*)-2-*naphthol.*

By A. BURAWOY and C. TURNER.

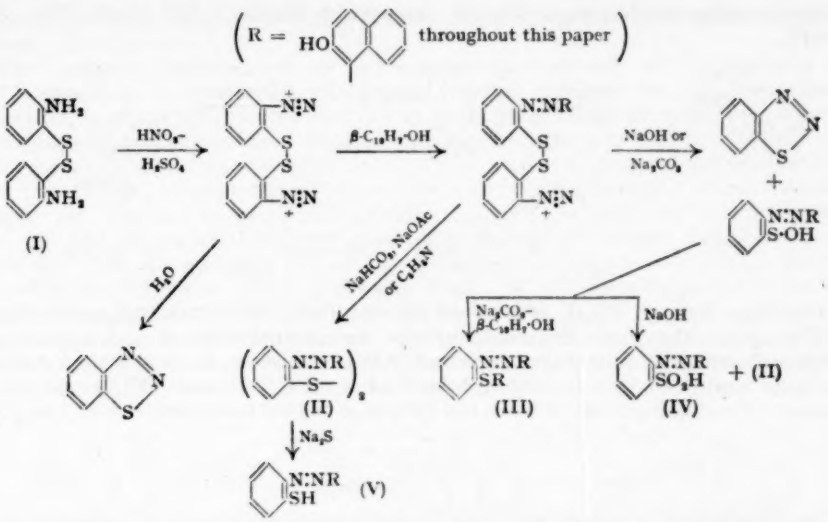
The tetrazonium salt from di-(2-amino-1-naphthyl) disulphide (VII) reacts with water much faster than its benzene analogue, forming naphtho(2′ : 1′-4 : 5)-1-thia-2 : 3-diazole (VIII). Coupling takes place when its concentrated sulphuric acid solution is added directly to alkaline β-naphthol, yielding only the sulphide (XI) and the naphthothiadiazole under all conditions. The disulphide (XV) is not obtained here. It is formed by treatment with sodium hydroxide of 2-(2-hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene (XIV) obtained by coupling diazotised 1-thiocyanato-2-naphthylamine (XIII) with β-naphthol. Reduction yields 1-(1-mercapto-2-naphthylazo)-2-naphthol (XVI). The oxidation and complex salt formation of the *o*-mercapto-azo-compounds are discussed.

A REPRESENTATIVE of the hitherto unknown *o*-mercapto-azo-compounds, 1-*o*-mercaptophenylazo-2-naphthol (V), was prepared from di-*o*-aminophenyl disulphide (I) by Burawoy and Turner (Part I *). This and reactions of the intermediates are represented in the first scheme on p. 1287.

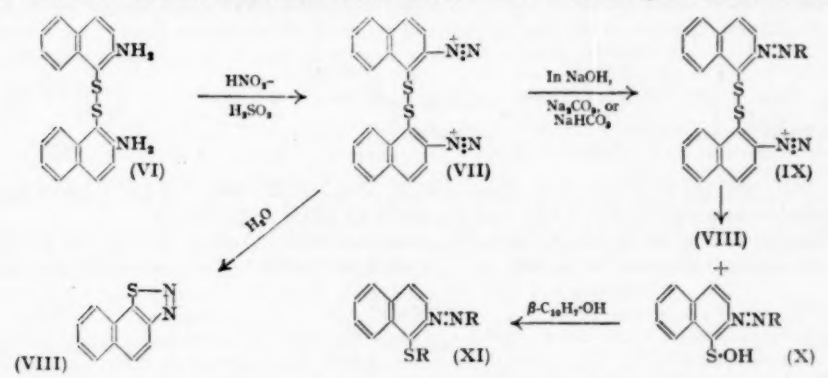
We have now attempted to prepare 1-(1-mercapto-2-naphthylazo)-2-naphthol (XVI) by the same method. In contrast to its analogue in the benzene series, however, the tetrazonium salt (VII) formed in concentrated sulphuric acid, *rapidly* decomposes on addition to water, yielding naphtho(2′ : 1′-4 : 5)-1-thia-2 : 3-diazole (VIII) in 50—60% yield. It does not couple with β-naphthol in sodium acetate, whereas in sodium hydroxide, sodium carbonate, or sodium hydrogen carbonate the red sulphide (XI) is isolated in good yield in addition to the naphthothiadiazole; however, the violet colour of the solutions of the crude product in organic solvents may indicate the formation of negligible amounts of the desired di-2-(2-hydroxy-1-naphthylazo)-1-naphthyl disulphide (XV).

These results indicate that the tetrazonium salt (VII), being less stable than its benzene analogue in presence of water, is hydrolysed in sodium acetate solution in preference to coupling with β-naphthol. In aqueous sodium hydroxide, sodium carbonate, or sodium hydrogen carbonate, one of the diazonium groups couples with one molecule of β-naphthol with sufficient rapidity, although the yields of naphthothiadiazole indicate partial decomposition of the tetrazonium salt. Coupling is followed by rapid decomposition of

* Part I, *J.*, 1950, 469.



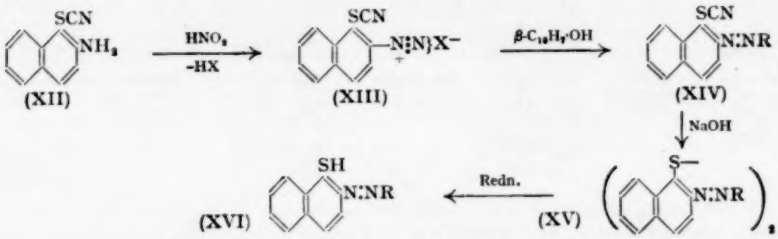
the monodiazonium intermediate (IX) to naphthothiadiazole and 2-(2-hydroxy-1-naphthylazo)-1-naphthalenesulphenic acid (X) which then reacts with another molecule of β-naphthol, a normal reaction of sulphenic acids, to yield 2-hydroxy-1-naphthyl 2-(2-hydroxy-1-naphthylazo)-1-naphthyl sulphide (XI). It is noteworthy that, in contrast to



its analogue in the benzene series, the sulphenic acid (X), in sodium hydroxide, reacts with another molecule of β-naphthol in preference to disproportionating to the disulphide and sulphinic acid.

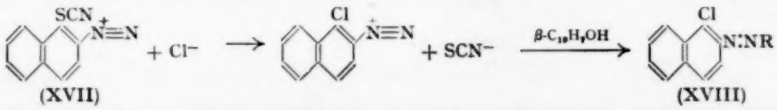
We therefore attempted an alternative method: the preparation of 2-(2-hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene (XIV) from 1-thiocyanato-2-naphthylamine (XII) by diazotisation and coupling with β-naphthol, and its conversion by sodium hydroxide into the desired disulphide (XV). Although we succeeded, the reactions proved rather complicated. 1-Thiocyanato-2-naphthylamine, after diazotisation in the usual manner in aqueous hydrochloric acid solution, coupled with β-naphthol to yield 1-chloro-2-(2-hydroxy-1-naphthylazo)naphthalene (XVIII) previously obtained by Morgan (*J.*, 1902, **81**, 1381) by the diazotisation of 1-nitro-2-naphthylamine in aqueous hydrochloric acid and coupling with β-naphthol. Exchange between the nuclear thiocyanato-group and the chlorine ion of 1-thiocyanatonaphthalene 2-diazonium chloride (XVII) had occurred. This is similar to the reverse rearrangement of *p*-chlorobenzenediazonium thiocyanate to

p-thiocyanatobenzenediazonium chloride observed by Hantzsch and Hirsch (*Ber.*, 1896, **29**, 947).



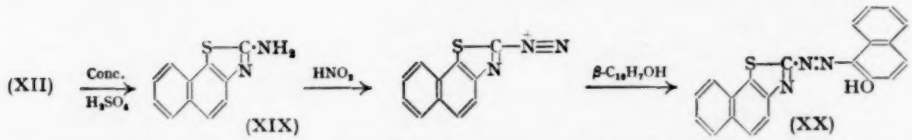
(XII) (XIII) (XIV) (XVI) (XV)

The diazonium salt (XIII) is obtained by diazotising 1-thiocyanato-2-naphthylamine (XII) in aqueous thiocyanic, dilute sulphuric, or concentrated sulphuric acid, coupling with β-naphthol giving the desired azo-compound (XIV). However, in concentrated sulphuric acid, some conversion into 2-aminonaphtho(2′ : 1′-4 : 5)-1 : 3-thiazole (XIX) could not be avoided. The diazonium salt of the latter substance yielded subsequently with β-naphthol



(XVII) (XVIII)

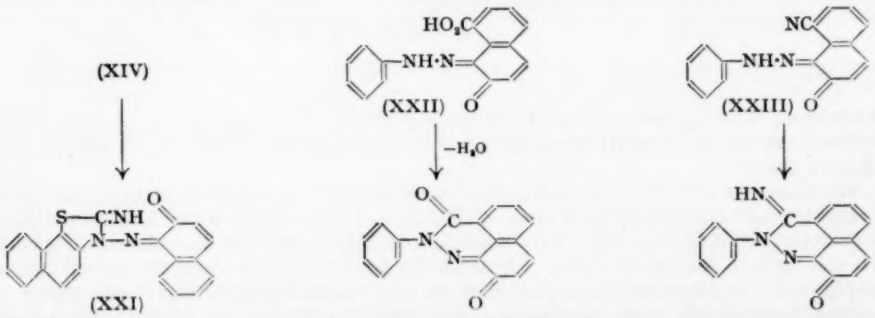
the azothiazole (XX), which was difficult to separate. When heated, the thiocyanato-compound (XIV) isomerises to a product which may be (XXI); and this on further heating decomposes to a high-melting substance of unknown constitution. This ring closure is similar to those observed by Willstätter, Ulbrich, Pogány, and Maimeri (*Annalen*, 1930,



(XIX) (XX)

477, 161) and by Burawoy and Markowitsch (*ibid.*, 1933, **504**, 71) for 1-phenylazo-2-naphthol-8-carboxylic acid (XXII) and its nitrile (XXIII) respectively.

Finally, 2-(2-hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene (XIV) was obtained pure as dark red prisms of m. p. 151° by rapid recrystallisation from a small amount of hot

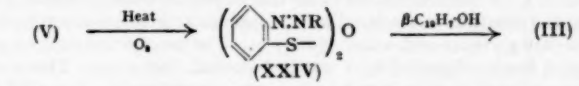


(XXI)

benzene, immediate filtration being essential. Quick treatment of its benzene solution with hot aqueous sodium hydroxide yields di-[2-(2-hydroxy-1-naphthylazo)-1-naphthyl] disulphide (XV) which dissolves in organic solvents with a characteristic violet colour and is reduced by hot alcoholic sodium sulphide to the violet-blue salt of 1-(1-mercapto-2-naphthylazo)-2-naphthol (XVI). The free red thiol is obtained by acidification of the

aqueous-alcoholic solution of this salt. It was characterised by the formation of the red *S*-methyl derivative.

The different behaviour of the *o*-mercapto-azo-compounds of the benzene and naphthalene series is noteworthy. As already reported in Part I (*loc. cit.*), 1-*o*-mercaptophenylazo-2-naphthol (V) is very sensitive to heat, being easily converted into a brown, alkali-insoluble product, which is obtained pure from hot xylene as bright red prisms. We have now established that this substance is *o*-(2-hydroxy-1-naphthylazo)benzenesulphenic anhydride (XXIV), by analysis and by conversion into the sulphide (III) when melted with β-naphthol. The fact that oxidation of this thiol gives the sulphenic anhydride rather than, as usually, the disulphide explains earlier failures to convert di-*o*-(2-hydroxy-1-naphthylazo)phenyl disulphide (II) into the thiol (V) by boiling it with alkaline alcoholic glucose or with alcoholic sodium hydroxide alone. At this high temperature, the thiol formed is easily oxidised to the sulphenic anhydride (XXIV); this spontaneously disproportionates in the presence of alkali to the sulphinic acid (IV) and the original disulphide which again reacts in the same manner until an almost quantitative yield of the sulphinic acid is obtained, as already reported.



(XXIV)

In contrast, the thiol (XVI) shows the usual behaviour, since it is very readily oxidised in air, particularly when dissolved in organic solvents or in alkaline conditions, yielding the disulphide (XV).

We have also prepared the copper, nickel, and cobalt complex salts of 1-*o*-mercaptophenylazo-2-naphthol and the copper and nickel salts of 1-(1-mercapto-2-naphthylazo)-2-naphthol. They possess the empirical formulæ $(C_{16}H_{11}ON_2S)_2M$ and $(C_{20}H_{13}ON_2S)_2M$ respectively. They are insoluble in water but slightly soluble in organic solvents such as benzene and chloroform. Their structures will be discussed elsewhere.

Experimental

Action of Water on Tetrazotised Di-(2-amino-1-naphthyl) Disulphide.—Di-(2-amino-1-naphthyl) disulphide (2 g.), dissolved in concentrated sulphuric acid (12 c.c.), was cooled to −5° and slowly added with stirring to nitrosylsulphuric acid (1 g. of sodium nitrite in 6 c.c. of concentrated sulphuric acid) in ice–salt. After 30 minutes, the solution was poured into ice water (500 c.c.). The yellow precipitate was filtered off and washed with water. Extraction with light petroleum (b. p. 60—80°) left an insoluble brown resin, m. p. 77—94° (0·6 g.). Evaporation of the solvent yields naphtho(2′ : 1′-4 : 5)-1-thia-2 : 3-diazole, m. p. 88—89° (1·2 g., 56%) (Jacobson and Schwartz, *Annalen*, 1893, **277**, 260, give 89°).

Coupling of Tetrazotised Di-(2-amino-1-naphthyl) Disulphide with β-Naphthol.—The disulphide (4 g.) in concentrated sulphuric acid (25 c.c.) was tetrazotised with nitrosylsulphuric acid (2 g. of sodium nitrite in 12 c.c. of concentrated sulphuric acid). The tetrazonium solution was added to a stirred solution of β-naphthol (20 g.), sodium hydroxide (6 g.), and sodium carbonate (150 g.) in ice and water (2500 g.). The precipitate was filtered off; after removal of the excess of β-naphthol with 3% aqueous sodium hydroxide (500 c.c.), the product was washed with water and finally digested with methyl alcohol (100 c.c.). The residue of *2-hydroxy-1-naphthyl 2-(2-hydroxy-1-naphthylazo)-1-naphthyl sulphide* (3·6 g., 66%) crystallised from xylene or glacial acetic acid as red prisms, m. p. 232—233° (Found: C, 75·0; H, 4·4; N, 6·2; residue, 1·8. $C_{30}H_{20}O_2N_2S$ requires C, 76·3; H, 4·3; N, 5·9%). It dissolves in organic solvents with an orange colour and in concentrated sulphuric acid with a dark violet colour rapidly changing to light brown. Evaporation of the methyl alcohol washings yielded the naphthothiadiazole, which was purified by dissolution in ether, removal of β-naphthol with 3% sodium hydroxide, and evaporation, giving material of m. p. 88—89° (2·3 g., 108%). Similar results were obtained by using sodium hydrogen carbonate or sodium hydroxide instead of sodium carbonate [Yields, in presence of sodium hydroxide: (XI), 2·3 g., 42%; naphthothiadiazole, 2·7 g., 1·26%]. No coupling took place in presence of sodium acetate.

Diazotisation of 1-Thiocyanato-2-naphthylamine in Hydrochloric Acid and Coupling with β-Naphthol.—1-Thiocyanato-2-naphthylamine (2 g.) in ethyl alcohol (200 c.c.) was poured into ice

and water (100 g.) and concentrated hydrochloric acid (20 c.c.). Sodium nitrite (1·0 g.) in a small amount of water was added. The orange diazonium solution was poured into an ice-cold aqueous solution (200 c.c.) of β-naphthol (3 g.) and sodium hydroxide (10 g.). The red precipitate formed was filtered off, washed with water, and crystallised from benzene and, finally, from glacial acetic acid. It was obtained as dark red prisms (3·2 g., 96%), m. p. 232—234°, alone or mixed with a sample of 1-(1-chloro-2-naphthylazo)-2-naphthol prepared as below (Found : C, 72·5; H, 4·1; N, 8·5; Cl, 10·1. Calc. for $C_{20}H_{13}ON_2Cl$: C, 72·3; H, 4·0; N, 8·4; Cl, 10·7%).

A solution of 1-chloro-2-naphthylamine hydrochloride (21·4 g.) in hot water (300 c.c.) and concentrated hydrochloric acid (35 c.c.) was cooled and, after addition of ice (200 g.), diazotised with sodium nitrite (7·5 g.) in a small amount of water. On addition to an aqueous ice-cold solution of β-naphthol (20 g.) and sodium hydroxide (25 g.) in water (600 c.c.), a red precipitate of the azo-compound (XVIII) separated. It was filtered off, washed with water, and recrystallised from glacial acetic acid, forming dark red prisms with a bronze lustre, m. p. 233—234°, in almost quantitative yield.

Diazotisation of 1-*Thiocyanato*-2-*naphthylamine in Concentrated Sulphuric Acid and Coupling with* β-*Naphthol.*—Finely powdered 1-thiocyanato-2-naphthylamine (10 g.) was slowly added to nitrosylsulphuric acid (8 g. of sodium nitrite in 80 c.c. of concentrated sulphuric acid) at −5°. After 1 hour's stirring the solution was poured into β-naphthol (30 g.), sodium hydroxide (10 g.), and sodium carbonate (240 g.) in ice and water (4000 g.). The precipitate formed was filtered off, washed with water, and finally digested with methyl alcohol (500 c.c.). The yield was 14·2 g. (80%). By rapid crystallisation from hot benzene, or concentration of a cold benzene solution under a vacuum, 2-(2-*hydroxy*-1-*naphthylazo*)-1-*thiocyanatonaphthalene* (XIV) was obtained as dark red prisms, m. p. 149·5—151° (Found : C, 71·2; H, 3·9; N, 12·1. $C_{21}H_{13}ON_3S$ requires C, 71·0; H, 3·7; N, 11·8%). It dissolves with a violet colour in concentrated sulphuric acid. By repeated crystallisations of the crude product from xylene, and removal of the insoluble decomposition products of 2-(2-hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene pure 2-(2-*hydroxy*-1-*naphthylazo*)*naphtho*(2′ : 1′-4 : 5)*thiazole* (XX) was obtained as aggregates of dark green needles, m. p. 240—242°, not depressed when the specimen was mixed with a pure sample prepared as below.

Diazotisation of 1-*Thiocyanato*-2-*naphthylamine in Thiocyanic Acid and Coupling with* β-*Naphthol.*—A solution of ammonium thiocyanate (100 g.) in an equivalent amount of 40% sulphuric acid at 0° was extracted with amyl alcohol (100 c.c.), and the alcoholic layer then extracted with ice-cold water (2 × 100 c.c.). The aqueous thiocyanic acid obtained was added at 0° to a solution of 1-thiocyanato-2-naphthylamine (5 g.) in ethyl alcohol (200 c.c.). This was treated with sodium nitrite (25 g.) in a small amount of water. The filtered orange diazonium solution was poured into an ice cold aqueous solution (1000 c.c.) of β-naphthol (15 g.), sodium hydroxide (5 g.), and sodium carbonate (80 g.). The precipitate was filtered off, washed with water, and digested with methyl alcohol (200 c.c.) (yield, 2·1 g., 24%). One crystallisation from benzene gave a product of m. p. 148—150°, identical with 2-(2-hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene described above.

Diazotisation of 1-*Thiocyanato*-2-*naphthylamine in Dilute Sulphuric Acid and Coupling with* β-*Naphthol.*—To a solution of 1-thiocyanato-2-naphthylamine (5 g.) in acetone (250 c.c.) and 10% sulphuric acid (200 c.c.) was added sodium nitrite (5 g.) in a small amount of water. The diazonium solution obtained was quickly poured into water and ice (1500 g.) containing β-naphthol (12 g.), sodium hydroxide (4 g.), and sodium carbonate (100 g.). The red precipitate was filtered off, washed with water, and digested with methyl alcohol (yield, 7·7 g., 87%). One crystallisation from benzene gave a product of m. p. 149—151°, alone or mixed with the foregoing product.

Action of Heat on 2-(2-*Hydroxy*-1-*naphthylazo*)-1-*thiocyanatonaphthalene.*—The compound was heated in toluene under reflux for 30 minutes. After cooling and filtration from a small amount of black insoluble matter, light petroleum was added, a *product* of m. p. 186—188° being precipitated, probably (XXI) (Found : C 70·9; H, 3·5; N, 12·0. $C_{21}H_{13}ON_3S$ requires C, 71·0; H, 3·7; N, 11·8%). It dissolves in concentrated sulphuric acid with a carmine colour. It has none of the properties of 2-(2-hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene; in particular, it cannot be converted by sodium hydroxide into di-[2-(2-hydroxy-1-naphthylazo)-1-naphthyl] disulphide. It could not be recrystallised, as further heating, such as boiling for 10 minutes in xylene, produced a black precipitate of m. p. about 340°, which only dissolved in hot glacial acetic acid containing some concentrated hydrochloric acid. By adding a larger amount of the latter acid a red *hydrochloride* with a green lustre crystallised (Found : C, 59·7;

H, 4·1; N, 6·9; Cl, 9·0. $C_{20}H_{14}O_3N_2S,HCl$ requires C, 60·2; H, 3·8; N, 7·0; Cl, 8·9%). Aqueous sodium hydroxide regenerates the original black compound, which dissolves in concentrated sulphuric acid with a violet colour which slowly fades with the formation of a red precipitate.

2-(2-*Hydroxy*-1-*naphthylazo*)*naphtho*(2′ : 1′-4 : 5)*thiazole*.—Well-powdered 2-aminonaphthothiazole (2 g.) was added to nitrosylsulphuric acid (1 g. of sodium nitrite in 25 c.c. of concentrated sulphuric acid). After 30 minutes at 0°, the solution was dropped into β-naphthol (10 g.), sodium hydroxide (3 g.), and sodium carbonate (100 g.) in ice and water (2000 g.). The precipitated *azo*-compound was filtered off, washed with water, and finally digested with methyl alcohol (200 c.c.) (yield, 1·1 g., 31%). Recrystallisation from glacial acetic acid gave aggregates of dark green needles containing one mol. of acetic acid of crystallisation, of m. p. 240—242°, which dissolved in organic solvents with a red-brown colour and in concentrated sulphuric acid with a pure blue colour (Found : C, 65·9; H, 4·4; loss on drying, 14·2. $C_{21}H_{13}ON_3S,CH_3·CO_2H$ requires C, 66·3; H, 4·1; loss on drying, 14·5. Found, after drying : C, 70·9; H, 3·9; N, 12·1. $C_{21}H_{13}ON_3S$ requires C, 71·0; H, 3·7; N, 11·8%).

Di-[2-(2-*hydroxy*-1-*naphthylazo*)-1-*naphthyl*] *Disulphide*.—2-(2-Hydroxy-1-naphthylazo)-1-thiocyanatonaphthalene (5 g.) was quickly dissolved in hot benzene (200 c.c.) and added to vigorously stirred 3% aqueous sodium hydroxide (500 c.c.) at 100°. After 5 minutes, the benzene was evaporated and the precipitate of nearly pure *disulphide* (4·5 g., 97%) filtered off and washed free from alkali. Recrystallisation from toluene gave dark green needles, m. p. 242—244°, which dissolve with a dark violet colour in organic solvents and an orange colour in concentrated sulphuric acid (Found : C, 73·3; H, 4·0; N, 8·6. $C_{40}H_{26}O_2N_4S_2$ requires C, 73·0; H, 4·0; N, 8·5%).

1-(1-*Mercapto*-2-*naphthylazo*)-2-*naphthol*.—The foregoing disulphide (3 g.), suspended in ethyl alcohol (250 c.c.), was heated under reflux with sodium sulphide nonahydrate (6 g.) in water (30 c.c.) for 1 hour. After cooling and filtration, the dark blue-violet solution obtained was treated with water (300 c.c.) and hydrochloric acid in excess. The red precipitate of 1-(1-*mercapto*-2-*naphthylazo*)-2-*naphthol* (2·85 g., 95%) was collected and washed with water. It crystallised from toluene (in absence of oxygen) and had m. p. 232—234° (Found : C, 72·4; H, 4·4; N, 8·4. $C_{20}H_{14}ON_2S$ requires C, 72·7; H, 4·3; N, 8·5%). It dissolves in organic solvents with an orange-red colour and in concentrated sulphuric acid with a violet-blue colour.

1-(1-*Methylthio*-2-*naphthylazo*)-2-*naphthol*.—The foregoing disulphide (1 g.), suspended in alcohol (80 c.c.), was heated under reflux with sodium sulphide nonahydrate (2 g.) in water (10 c.c.) for 1 hour and then cooled. Water (100 c.c.) was added, followed by three portions of 10% aqueous sodium hydroxide (5 c.c. each) and methyl sulphate (1·4 c.c. each), with vigorous shaking. The red precipitate of 1-(1-*methylthio*-2-*naphthylazo*)-2-*naphthol* formed quantitatively was filtered off and washed with water. Recrystallisation from glacial acetic acid gave red needles with a green lustre, m. p. 174—175°, which dissolve in organic solvents with an orange colour and in concentrated sulphuric acid with a violet colour (Found : C, 73·3; H, 4·7; N, 8·1. $C_{21}H_{16}ON_2S$ requires C, 73·2; H, 4·7; N, 8·1%).

Oxidation of 1-o-*Mercaptophenylazo*-2-*naphthol to* o-(2-*Hydroxy*-1-*naphthylazo*)*benzenesulphenic Anhydride*.—Attempts to recrystallise 1-*o*-mercaptophenylazo-2-naphthol from organic solvents (acetone, benzene, toluene) yielded the sparingly soluble o-(2-*hydroxy*-1-*naphthylazo*)*benzenesulphenic anhydride* (XXIV) (cf. Part I of this series), bright red prisms, m. p. 241—243° (from xylene or chlorobenzene), giving orange solutions in organic solvents and a violet colour in concentrated sulphuric acid (Found : C, 66·8; H, 3·8; N, 10·0. $C_{32}H_{22}O_3N_4S_2$ requires C, 66·9; H, 3·9; N, 9·8%).

Condensation of o-(2-*Hydroxy*-1-*naphthylazo*)*benzenesulphenic Anhydride with* β-*Naphthol*.—The anhydride (0·5 g.) and β-naphthol (1·0 g.) were heated together at 120° for 1 hour, the liquid mass becoming semi-solid. After cooling, it was digested with a little methyl alcohol, filtered off, and washed (0·65 g., 89%). One recrystallisation from xylene and a little charcoal gave brownish-red needles, m. p. 226—227°, not depressed by admixture of the compound with 2-hydroxy-1-naphthyl *o*-(2-hydroxy-1-naphthylazo)phenyl sulphide prepared by coupling tetrazotised di-*o*-aminophenyl disulphide and β-naphthol in aqueous sodium carbonate (cf. Part I of this series).

Oxidation of 1-(1-*Mercapto*-2-*naphthylazo*)-2-*naphthol*.—1-(1-Mercapto-2-naphthylazo)-2-naphthol (0·2 g.) in toluene (50 c.c.) was heated under reflux for 2 hours while a stream of oxygen passed through the solution. On concentration to a small volume, di-[2-(2-hydroxy-1-naphthylazo)-1-naphthyl] disulphide (0·13 g.), m. p. 241—243°, crystallised. The m. p. was not depressed when the sample was mixed with one obtained directly by the action of sodium hydroxide on

2-(2-hydroxy-1-naphthylazo)thiocyanatonaphthalene, and the product gave an orange colour in concentrated sulphuric acid.

When a solution of 1-(1-mercapto-2-naphthylazo)-2-naphthol in alcoholic sodium hydroxide was shaken for a few minutes, di-[2-(2-hydroxy-1-naphthylazo)-1-naphthyl] disulphide was quantitatively precipitated. One recrystallisation from toluene yielded a pure product of m. p. 242—244°.

Metallic Complex Salts of 1-(o-*Mercaptophenylazo*)-2-*naphthol.—Copper.* To a filtered solution of the sodium salt of 1-(*o*-mercaptophenylazo)-2-naphthol (0·5 g.) in ethyl alcohol (200 c.c.) were added water (300 c.c.), followed by an aqueous solution of copper sulphate pentahydrate (0·5 g.). The brown *salt* precipitated was filtered off and washed with water. It (0·35 g., 63%) had m. p. 306—308° (Found: Cu, 10·0. $C_{32}H_{22}O_2N_4S_2Cu$ requires Cu, 10·2%). The complex is slightly soluble in acetone, chloroform, and benzene, giving orange solutions, and insoluble in water, ethyl alcohol, and light petroleum.

Cobalt. This *salt* (0·40 g., 73%), m. p. 285—288°, was prepared similarly, a solution of cobalt sulphate being added (Found: Co, 9·2. $C_{32}H_{22}O_2N_4S_2Co$ requires Co, 9·6%). It is slightly soluble in acetone, chloroform, and benzene, giving dark brown solutions, and insoluble in water, ethyl alcohol, and light petroleum.

The *nickel* salt (yield, 55%) had m. p. 334—337° (Found: Ni, 9·5. $C_{32}H_{22}O_2N_4S_2Ni$ requires Ni, 9·6%). It is slightly soluble in chloroform and benzene, giving orange-brown solutions, and insoluble in water, ethyl alcohol, acetone, and light petroleum.

Metallic Complex Salts of 1-(1-*Mercapto*-2-*naphthylazo*)-2-*naphthol.—Copper.* To a filtered solution of 1-(1-mercapto-2-naphthylazo)-2-naphthol (0·3 g.) in acetone (200 c.c.) was added copper sulphate pentahydrate (0·3 g.) in water (300 c.c.). The brown salt (0·20 g., 61%), m. p. 256—258°, precipitated was filtered off and washed with water (Found: Cu, 9·1. $C_{40}H_{26}O_2N_4S_2Cu$ requires Cu, 8·8%). It is slightly soluble in acetone, chloroform, and benzene, giving purple solutions.

The *nickel* salt, prepared similarly in 73% yield, had m. p. 300—302° (Found: Ni, 8·1. $C_{40}H_{26}O_2N_4S_2Ni$ requires Ni, 8·2%) and was slightly soluble in acetone, chloroform, and benzene, giving red solutions.

Both salts are insoluble in water, ethyl alcohol, and light petroleum.

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233. *The Heats of Formation of Germanium Tetrabromide and Germanium Tetraiodide.*

By D. F. EVANS and R. E. RICHARDS.

The heats of solution of germanium tetrabromide and tetraiodide, and of germanium dioxide in 1·2N-sodium hydroxide solution have been measured. From these results the heats of formation of the two tetrahalides have been deduced. The bond energies and stabilisation energies of the Ge–Br and the Ge–I link in these compounds are also given.

OF the germanium tetrahalides, the chloride is the only one for which reliable thermochemical data are available. Roth and Schwartz (*Z. physikal. Chem.*, 1928, **134**, 456) determined the heat of formation from the heat of hydrolysis in water to give germanium dioxide (colloidal) and hydrochloric acid. Since only one of their experiments was successful owing to separation of solid germanium dioxide, and since the heat of formation of a colloidal solution of germanium dioxide is probably less accurately known than that of solid GeO_2, a modified procedure has been used in these measurements. The heats of solution of germanium tetrabromide and tetraiodide in 1·2N-sodium hydroxide to give sodium germanate and sodium halide were measured, and combined with the heat of solution of GeO_2 in the same solvent.

EXPERIMENTAL

Commercial germanium tetrabromide was fractionally crystallised in a sealed vessel, and then had m. p. 26° (Dennis and Hance, *J. Amer. Chem. Soc.*, 1922, **44**, 299, give 26·1°). Germanium tetraiodide, prepared by the method of "Inorganic Syntheses," Vol. II, p. 112, and twice recrystallised from chloroform, had m. p. 146°. A pure specimen of germanium dioxide from Messrs. Johnson Matthey was used without further purification.

The calorimetric measurements were made with a modified form of the adiabatic calorimeter described by Cottrell and Wolfenden (*J.*, 1948, 1019). The solvent was placed in the cylindrical silver calorimeter, and the sample was contained in a small glass tube mounted on a silver frame inside the calorimeter. The open end of the glass tube was ground flat, and a mica lid was fastened to the end of the tube by a thin film of oil, and when the calorimeter rotated, this lid was dislodged by a glass-coated weight. Experiments made with thin glass lids, and greases of various kinds, showed that a much heavier weight was required to dislodge the lid. This was unsatisfactory as it gave rise to large and irregular heats of stirring. The glass tube, sealed as described with a mica lid, showed no gain in weight during 12 hours, when filled with calcium chloride and kept in an atmosphere saturated with water vapour. The calorimeter was calibrated by means of the heat of solution of solid potassium chloride in water, the following value being assumed :

$$KCl(solid) + 200H_2O = KCl,200H_2O;\ \Delta H = 4{\cdot}201 \text{ kcal. at } 25°$$

(" Selected Values of Chemical Thermodynamic Properties," National Bureau of Standards, 1948.) The heat of hydrolysis of germanium tetraiodide was also measured with a twin calorimeter of high sensitivity, electrical calibration being used. The sample was contained in a sealed glass bulb which was broken at the beginning of the experiment. A description of this calorimeter will be published later.

The heat of the reaction $Ge(solid) + O_2 = GeO_2(solid)$ has been measured by Becher and Roth (*Z. physikal. Chem.*, 1932, *A*, **161**, 69; 128·1 kcal.) and by Hahn and Juza (*Z. anorg. Chem.*, 1940, **244**, 111; 128·6 kcal.). The value given in the " Selected Tables of Thermodynamic Properties," *viz.*, 128·3 kcal., was accordingly adopted. The heats of formation of sodium hydroxide, iodide, and bromide in solution were also taken from the same source (the difference between the heats of formation of the halides in water and in 1·2N-sodium hydroxide solution being assumed to be small), and also the heats of vaporisation, sublimation, or dissociation of germanium (78·44 kcal./g.-atom) and germanium tetrabromide, bromine, and iodine. The heat of sublimation of germanium tetraiodide was assumed to be the same as for tin tetraiodide, which has very similar m. p. and b. p.

The results are given in the following table, from which we have

$$Ge(solid) + 2Br_2(liquid) = GeBr_4(liquid);\ \text{mean } \Delta H = -78{\cdot}5 \text{ kcal./mole}$$
$$Ge(solid) + 2I_2(solid) = GeI_4(solid);\ \text{mean } \Delta H = -30{\cdot}5 \text{ kcal./mole}$$

Whence bond energy of Ge–Br link = 63·5 kcal./mole, and of Ge–I link = 48·1 kcal./mole.

Wt. of Ge compd., g.	Wt. of 1·2N-NaOH, aq., g.	Δt	Final temp.	$-\Delta H$, kcal./mole
	Heat of hydrolysis of germanium tetrabromide (liquid).			
0·2948	52·10	0·905°	27·4°	92·0
0·2358	52·12	0·721	27·3	91·6
0·2008	52·10	0·611	27·2	91·4
	Heat of hydrolysis of germanium tetraiodide (solid).			
0·1990	52·20	0·3486	27·1	78·0
0·06870 *	*ca.* 305	—	25·0	77·3
	* Second measurement made with twin calorimeter.			
	Heat of solution of germanium dioxide in 1·2N-sodium hydroxide solution.			
0·0778	52·12	0·0936	26·7	9·50

Discussion.—If the bond energy of a pure covalent bond A–B is defined as the arithmetic mean of the bond energies of A_2 and B_2, then one-quarter of the heats of formation of the gaseous germanium (or silicon) tetrahalides from solid germanium or silicon and gaseous halogen is equal to the stabilisation energies of the M–halogen bond due to such factors as ionic character and possibly double-bond character (Pauling, " Nature of the Chemical Bond," 2nd edn., p. 61). The heats of formation of gaseous germanium tetrabromide and tetraiodide together with those for other gaseous tetrahalides are given below. The additional thermodynamical data are from " Selected Values, etc." (see above), except the heat of sublimation of silicon tetraiodide which is an estimated one (Brewer, in " The Chemistry and Metallurgy of Miscellaneous Materials," edited by Quill).

Heats of formation (kcal./mole) of gaseous compounds from solid metals and gaseous halogens.

$SiCl_4$	145·7	$SiBr_4$	100·7	SiI_4	47·7
$GeCl_4$	122	$GeBr_4$	83·3	GeI_4	42·6

It is noteworthy that the stabilisation energies are less for germanium halides than for silicon halides, indicating that the simple interpretation of these bonds in terms of ionic and covalent character is incomplete, since on this basis alone the converse might be expected.

A similar situation is found in the observed bond contractions (sum of covalent radii minus actual bond distance) for silicon–halogen and germanium–halogen links, which are usually greater in the former than in the latter. This is clearly shown in accurate microwave measurements (Sheridan and Gordy, *J. Chem. Physics*, 1951, **19**, 965).

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234. *Reaction of Primary Amines with o-Hydroxydibenzoylmethanes, and the Preparation of Derivatives of Flavone Imine.*

By WILSON BAKER, J. B. HARBORNE, and W. D. OLLIS.

Reaction of benzylamine with 3-benzoylflavone gives *N*-benzylbenzamide and the yellow 2-β-benzylaminocinnamoylphenol (IV; R = Ph), but the latter is obtained only in traces from benzylamine and *o*-hydroxydibenzoylmethane, the main product being a colourless isomeride now shown to be 2-hydroxyflavanone benzylimine (VII). This hydroxyflavanone is readily dehydrated under acid conditions to give flavone benzylimine (IX), and this and other derivatives of flavone alkyl- or aryl-imines resist acid hydrolysis. The flavone imines may also be prepared by reaction of 4-thionflavone, or more readily 4-thionflavone methiodide, with primary bases. The flavone alkylimines react with excess of hydrogen sulphide to give 4-thionflavone, and are converted into flavones by reaction of their methiodides with alkali.

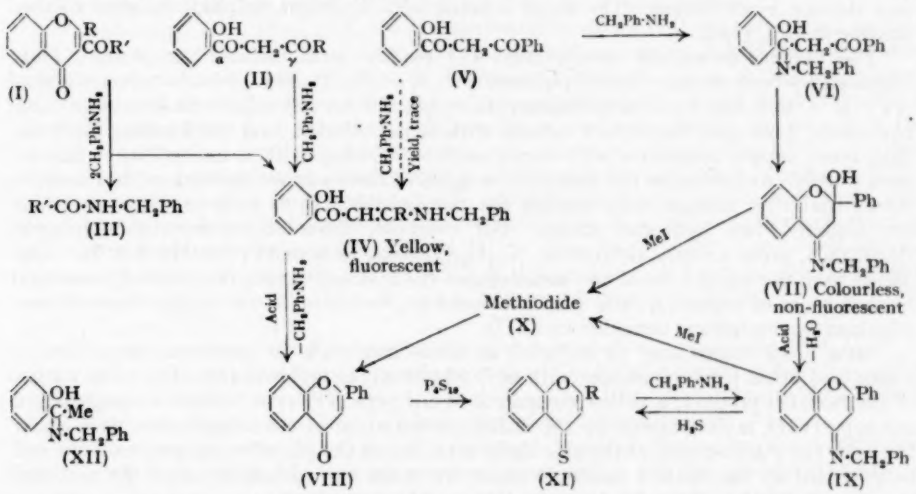
An attempt has been made to determine the factors governing the relative reactivity of the two carbonyl groups in substituted *o*-hydroxydibenzoylmethanes (XIII) by studying their reaction with benzylamine. Observations have been made on the anhydroacetyl derivatives of acyl-*o*-hydroxybenzoylmethanes which are all found to be derivatives of 2-methylchromone, and on some " diflavones."

REACTION of an *o*-hydroxyacetophenone with the anhydride and sodium salt of an aliphatic or aromatic acid gives a 3-acyl-2-alkyl- or -aryl-chromone (I; R = R′ = alkyl or aryl), and these compounds are similarly formed from the 1 : 3-diketones (II; R = alkyl or aryl) (see Baker, *J.*, 1933, 1381; Baker and Butt, *J.*, 1949, 2142, where references to earlier work are given). If, in the 1 : 3-diketone (II), R is a different radical from that in the acid R′·CO_2H whose anhydride and sodium salt are employed, then the 3-acylchromone produced may be either (I) or the isomer where R and R′ are interchanged, since a triacylmethane is involved as an intermediate. Although hydrolysis cannot be relied upon to distinguish between these isomerides owing to the possibility of ring opening, Baker and Butt (*loc. cit.*) and Baker and Glockling (*J.*, 1950, 2759) have shown that reaction with benzylamine serves to differentiate between them by cleavage of the 3-acyl group as an acylbenzylamide (III) and formation of a yellow, highly fluorescent, unsaturated ketone (IV; R = alkyl or aryl). The ketones (IV) where R is an alkyl group derived from a 3-acyl-2-alkylchromone may also be prepared by direct condensation of benzylamine with an alcoholic solution of the 1 : 3-diketone (II; R = alkyl) (Baker and Butt, *loc. cit.*).

The reactions are not quite the same in the 2-arylchromone (flavone) series. Thus, although 3-benzoylflavone (I; R = R′ = Ph) yielded *N*-benzylbenzamide (III; R′ = Ph) and the yellow, fluorescent 2-β-benzylaminocinnamoylphenol (IV; R = Ph) (Baker and Glockling, *loc. cit.*), it has now been found that only a trace of (IV; R = Ph) is obtained from *o*-hydroxydibenzoylmethane (V) and benzylamine, the main product being a colourless,

non-fluorescent, non-phenolic compound isomeric with (IV; R = Ph). The present investigation is concerned mainly with the nature of the reactions between primary amines and *o*-hydroxyphenyl-1 : 3-diketones (II). Reference may be made to the article by Cromwell (*Chem. Reviews*, **1946**, **38**, 90) which deals *inter alia* with the reaction of amines with 1 : 3-diketones. The work now described appears to afford the first instance of the condensation of a primary amine with a 1 : 3-diketone to give two isomeric products arising from reaction at each of the carbonyl groups.

2-β-Benzylaminocinnamoylphenol (IV; R = Ph) prepared from 3-benzoylflavone (I; R = R′ = Ph), and its colourless isomeride prepared from *o*-hydroxydibenzoylmethane (V) are not interconvertible, thus excluding the unlikely possibilities that they might be either polymorphs or enamine and ketimine isomerides. The representation of (IV) as an enamine rather than as its, probably tautomeric, ketimine form, is preferable on account of its intense yellow colour and fluorescence, which indicate a high degree of conjugation. The colourless compound is hence a structural isomeride of (IV; R = Ph), and it appeared probable that it had been formed by condensation of benzylamine with the carbonyl group attached to the phenolic nucleus in (V) to give first the Schiff's base (VI), which then undergoes cyclisation to the non-phenolic semi-acetal (VII). This view of the structures of the yellow and the colourless isomeride as (IV; R = Ph) and (VII) respectively has now been established by a study of both compounds.



The yellow, fluorescent compound (IV; R = Ph) when heated with acetic acid and a little hydrochloric acid at 100° (conditions used for the cyclisation of *o*-hydroxydibenzoylmethanes to flavones) gave benzylamine hydrochloride and flavone (VIII) in high yield. Under the same conditions the colourless, isomeric compound (VII) underwent dehydration, giving the sparingly soluble hydrochloride of a base, $C_{22}H_{17}ON$. This base is flavone benzylimine (IX); it is also formed from (VII) by heating it with glacial acetic acid, and is obtained as its picrate by treating (VII) with ethanolic picric acid. A more direct synthesis of flavone benzylimine (IX) is by heating 4-thionflavone (XI; R = Ph; see the following paper) with benzylamine in alcoholic solution, and it is also produced under very mild conditions from 4-thionflavone methiodide (following paper) and benzylamine. The reaction between 4-thionflavone and benzylamine is reversible; when flavone benzylimine is treated with hydrogen sulphide in alcoholic solution, 4-thionflavone separates in 72% yield. Flavone benzylimine (IX) gives a yellow methiodide (X), also obtained from (VII) by heating it with methanolic methyl iodide; (X) is hydrolysed by warming it with aqueous methanol and a trace of sodium hydroxide, giving flavone (VIII) and, unexpectedly, benzylamine as the only isolable base. The structure of this methiodide has not been

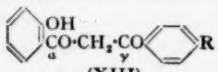
established; if it is a simple quaternary methiodide its hydrolysis must be accompanied by at least partial loss of the methyl group from the nitrogen atom. Flavone benzylimine is stable to hot hydrochloric acid, an abnormal behaviour for a Schiff's base. The stability may be connected with the electromeric change, —O—CPh=CH—C=N—, which is possible in flavone benzylimine and would be expected to reduce the chemical reactivity of the —C=N— group.

The dehydration of the non-fluorescent compound to give flavone benzylimine (IX), coupled with the facts that it is non-phenolic, being insoluble in aqueous sodium hydroxide, and that it gives neither a ferric chloride reaction nor a derivative with copper acetate, proves that it is 2-hydroxyflavanone benzylimine (VII). The formation of this cyclic semi-acetal from (VI) has a close parallel in the cyclisation of ketose sugars to pyranose forms, and it is likely that such compounds are involved in the ring closure of acyl-*o*-hydroxybenzoylmethanes (II) to chromones and flavones.

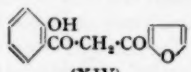
A similar colourless, non-fluorescent compound was obtained from *o*-hydroxydibenzoylmethane (V) by reaction with *n*-butylamine. This 2-hydroxyflavanone *n*-butylimine was dehydrated by warm acetic acid to flavone *n*-butylimine, which proved to be identical with a specimen prepared from 4-thionflavone and *n*-butylamine. A similar series of reactions employing *n*-octylamine gave the colourless 2-hydroxyflavanone *n*-octylimine and flavone *n*-octylimine. The latter reacted with hydrogen sulphide to give 4-thionflavone in 91% yield.

The yellow, fluorescent compounds (IV) readily form metallic complexes. Thus, although 2-β-benzylaminocinnamoylphenol (IV; R = Ph), 2-β-benzylaminocrotonoylphenol (IV; R = Me), and 2-β-*n*-hexylaminocrotonoylphenol are not soluble in aqueous sodium hydroxide, they give deep green colours with ferric chloride, and yield rather insoluble, dark green copper complexes with cupric acetate. Owing to their insolubility it has not been possible to determine the molecular weights of these copper derivatives, but analysis shows that they unexpectedly contain one molecule of (IV) to each copper atom which has replaced two hydrogen atoms. For example, 2-β-*n*-hexylaminocrotonoylphenol, $C_{16}H_{23}O_2N$, gives a cupric derivative, $(C_{16}H_{21}O_2NCu)_n$ (*n* is most probably 2 or 3). This differs from the usual ratio of two molecules of the hydroxy-carbonyl or related compound to each atom of copper, a ratio which is found in, for example, the copper derivative of *o*-hydroxyacetophenone benzylimine (XII).

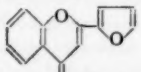
Some observations may be recorded in connection with the condensation of benzylamine and other primary amines with acyl-*o*-hydroxybenzoylmethanes (II). The nature of the reaction product, a yellow compound of the type (IV) or a colourless compound of the type (VII), is determined by the initial condensation of the benzylamine with either the α- or the γ-keto-group of the side chain attached to the phenolic nucleus, and this will be governed by the relative cationoid character of the two carbon atoms of the carbonyl groups, possibly by effects due to enolisation, and by steric factors.



(XIII)



(XIV)



(XV)

With acetyl-*o*-hydroxybenzoylmethane (II; R = Me) condensation occurs exclusively at the γ-carbonyl group, which is undoubtedly the more cationoid of the two and the less subject to steric effects, giving (IV; R = Me). With *o*-hydroxydibenzoylmethane (XIII; R = H) containing a less reactive γ-carbonyl group, the condensation takes place mainly at the α-carbonyl group, giving 2-hydroxyflavanone benzylimine (VII) in 79% yield and only a 1% yield of (IV; R = Ph). *o*-Hydroxy-*p'*-methoxydibenzoylmethane (XIII; R = OMe) with an even less cationoid γ-carbonyl group reacts exclusively at the α-carbonyl group to give 2-hydroxy-4'-methoxyflavanone benzylimine. *p*-Chloro-*o'*-hydroxydibenzoylmethane (XIII; R = Cl) reacts almost exclusively at the α-carbonyl group to give 4'-chloro-2-hydroxyflavanone benzylimine, but the yellow colour of the

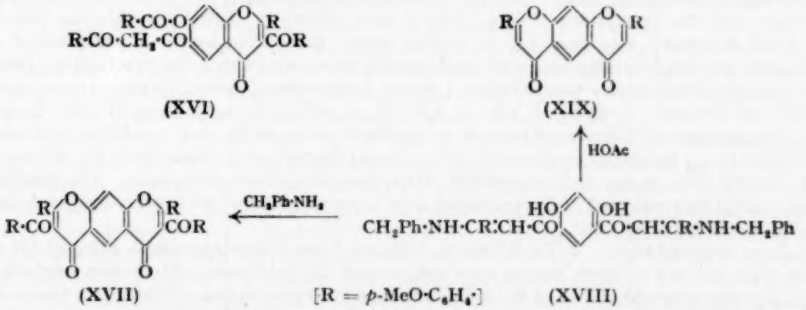
reaction mixture indicates the presence of a trace of (IV; R = *p*-Cl·C_6H_4), but this could not be isolated. Broadly speaking, these results are in accord with expectations, but it is clear from the work of Lapworth and Manske (*J.*, 1928, 2533), who studied the stability of aromatic aldehyde cyanohydrins, that no simple relation exists between the cationoid properties of the carbonyl group and the expected electronic effects of substituents in the aromatic nucleus. Again, Bradley and Robinson (*J.*, 1926, 2356) found that the interpretation of the hydrolysis of substituted dibenzoylmethanes was not simple, and this was also found to be the case for the reaction of hydroxylamine with dibenzoylmethanes (Shenoi, Shah, and Wheeler, *J.*, 1940, 247).

2-Hydroxy-4′-methoxyflavanone benzylimine and 4′-chloro-2-hydroxyflavanone benzylimine (cf. VII) were dehydrated by acetic acid at 100° to give 4′-methoxy- and 4′-chloro-flavone benzylimines, respectively (cf. IX); these flavone alkylimines readily gave picrates. *o*-Hydroxy-*p*′-nitrodibenzoylmethane (XIII; R = NO_2) reacted differently with benzylamine giving, in methanolic solution, a small yield of 4′-nitroflavone by direct cyclisation, but the main reaction was cleavage of the molecule with formation of methyl *p*-nitrobenzoate and *o*-hydroxyacetophenone benzylimine (XII). 2-Hydroxy-4 : 6-dimethoxydibenzoylmethane did not react with benzylamine under the conditions employed. 2-Furoyl-*o*-hydroxybenzoylmethane (XIV) reacted with benzylamine at the α-carbonyl group, giving the colourless 2-2′-furyl-2-hydroxychromanone benzylimine, which was dehydrated by acetic acid to 2-2′-furylchromone benzylimine (XV).

Anhydroacetyl Derivatives of Acyl-o-hydroxybenzoylmethanes.—It appears to be a general rule that if a diketone (II; R = alkyl or aryl) is heated with acetic anhydride and sodium acetate, the product is a 3-acyl derivative of 2-methylchromone. Thus, anhydroacetylation of *o*-hydroxydibenzoylmethane and of 4-methyl-2-propionoacetylphenol gives 3-benzoyl-2 methylchromone and 2 : 6-dimethyl-3-propionylchromone respectively, the nature of the products having been established by reaction with benzylamine (Baker and Butt, *loc. cit.*). Two further examples have now been found. 2-Furoyl-*o*-hydroxybenzoylmethane (XIV), acetic anhydride, and sodium acetate give 3-2′-furoyl-2-methylchromone; this reacts with benzylamine to give 2-β-benzylaminocrotonoylphenol (IV; R = Me). Anhydroacetylation of *o*-hydroxy-*p*′-nitrodibenzoylmethane (XIII; R = NO_2) gives 2-methyl-3-*p*-nitrobenzoylchromone (I; R = Me; R′ = *p*-NO_2·C_6H_4), giving with benzylamine 2-β-benzylaminocrotonoylphenol (IV; R = Me) and *N*-benzyl-*p*-nitrobenzamide, *p*-NO_2·C_6H_4·CO·NH·CH_2Ph.

The same tendency to give 2-methylchromones is shown by the facts that (*a*) 2 : 6-dimethyl-3-propionylchromone is the sole product of the propionylation of 2-acetoacetyl-4-methylphenol (Baker and Butt, *loc. cit.*), and (*b*) 2-acetoacetylphenol reacts with benzoic anhydride and triethylamine to give 3-benzoyl-2-methylchromone (this paper).

The Structure of Some Derivatives of "Diflavone."—Algar, McCarthy, and Dick (*Proc. Roy. Irish Acad.*, 1933, **41**, 155) proposed structure (XVI) for the product obtained by



fusing 4 : 6-diacetylresorcinol with *p*-methoxybenzoic anhydride and sodium *p*-methoxybenzoate (Allan and Robinson's flavone synthesis). This reaction has now been repeated, and has also been carried out with *p*-methoxybenzoic anhydride in triethylamine (cf.

Kuhn and Low, *Ber.*, 1944, **77**, 202). In each case, the same product was isolated, but the yield was much better from the latter reaction.

The structure (XVII) assigned to the product was proved by reaction with benzylamine, which gave the strongly fluorescent 4 : 6-di-(β-benzylamino-4-methoxycinnamoyl)resorcinol (XVIII) and *N*-benzyl-*p*-methoxybenzamide $MeO{\cdot}C_6H_4{\cdot}CO{\cdot}NH{\cdot}CH_2Ph$. This behaviour is analogous to that of other 3-aroylflavones (see Baker and Glockling, *loc. cit.*). The 4 : 6-di-(β-benzylamino-4-methoxycinnamoyl)resorcinol was cyclised by acetic–hydrochloric acids, with loss of benzylamine, giving "4 : 4'-dimethoxydiflavone" (XIX) previously described by Algar, McCarthy, and Dick (*loc. cit.*).

Experimental

M.p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

2-β-*Benzylaminocinnamoylphenol* (IV; R = Ph).—The following method is more satisfactory than that described by Baker and Glockling (*loc. cit.*). 3-Benzoylflavone (5·9 g.), benzylamine (4·4 c.c.), and dry pyridine (45 c.c.) were heated under reflux for 20 hours, cooled, and poured into dilute acetic acid. The precipitate was collected and crystallised from ethanol, giving 2-β-benzylaminocinnamoylphenol (4·7 g., 79%) as yellow needles, m. p. 96—98° (lit., m. p. 98°). Its alcoholic solution gave a deep green colour with ferric chloride.

2-*Hydroxyflavanone Benzylimine* (VII).—*o*-Hydroxydibenzoylmethane (2·5 g.), benzylamine (1·25 c.c.), and ethanol (25 c.c.) were heated for 2·5 hours and cooled, and the precipitate (2·7 g., 79%), m. p. 170° (decomp.), was collected and crystallised from ethanol (150 c.c.), giving 2-*hydroxyflavanone benzylimine* as colourless prisms, m. p. 175° (decomp.) (Found: C, 80·1; H, 5·5; N, 4·3. $C_{22}H_{19}O_2N$ requires C, 80·2; H, 5·8; N, 4·3%). It is not fluorescent in ultra-violet light, is insoluble in aqueous sodium hydroxide, and gives no colour with ferric chloride or derivative with ethanolic cupric acetate.

Concentration of the original, fluorescent alcoholic mother-liquors and crystallisation of the product from ethanol gave 2-β-benzylaminocinnamoylphenol (42 mg., 1%), m. p. and mixed m. p. 96—98°.

Reaction of 2-β-Benzylaminocinnamoylphenol with Acetic–Hydrochloric Acid. Formation of Flavone and Benzylamine.—A mixture of 2-β-benzylaminocinnamoylphenol (IV; R = Ph) (642 mg.), glacial acetic acid (10 c.c.), and concentrated hydrochloric acid (1 c.c.) was heated on a steam-bath for 10 minutes and poured into water. After cooling to 0°, the crystalline precipitate (390 mg., 90%) was collected, washed, dried, and crystallised from light petroleum (b. p. 60—80°), giving flavone, m. p. and mixed m. p. 96—97°.

The original aqueous mother-liquors were evaporated under diminished pressure and the residue was washed with ether and dried, giving benzylamine hydrochloride (81 mg., 29%), m. p. and mixed m. p. 256°.

Flavone Benzylimine (IX).—(a) *Dehydration of 2-hydroxyflavanone benzylimine by acetic–hydrochloric acid.* A mixture of 2-hydroxyflavanone benzylimine (1 g.), glacial acetic acid (10 c.c.), and concentrated hydrochloric acid (1 c.c.) was heated on a steam-bath for 10 minutes, then poured into water, and the precipitate (1·05 g., 100%) was collected. This hydrochloride (250 mg.), m. p. 270° (decomp.), was dissolved in boiling water, 2N-sodium hydroxide was added until the mixture was slightly alkaline, and after cooling in a refrigerator the precipitate (160 mg., 71%) was crystallised from aqueous ethanol, giving *flavone benzylimine* (IX) as colourless needles, m. p. 95—96° (Found: C, 84·5; H, 5·6; N, 4·6. $C_{22}H_{17}ON$ requires C, 84·9; H, 5·5; N, 4·5%).

(b) *Dehydration of 2-hydroxyflavanone benzylimine with acetic acid.* 2-Hydroxyflavanone benzylimine (1 g.) in glacial acetic acid (10 c.c.) was heated on a steam-bath for 10 minutes, cooled, poured into water, and neutralised with aqueous sodium carbonate. The precipitate (860 mg., 90%) was collected and crystallised from aqueous ethanol, giving flavone benzylimine, m. p. and mixed m. p. 95—96°.

(c) *From 4-thionflavone.* 4-Thionflavone (100 mg.; see following paper), ethanol (10 c.c.), and benzylamine (1 c.c.) were heated on a steam-bath for 2·5 hours. Hydrogen sulphide was evolved and the deep-red colour of the 4-thionflavone gradually faded. Water was then added, and the precipitate collected and crystallised from aqueous ethanol, giving flavone benzylimine (124 mg., 95%), m. p. and mixed m. p. 95—96° (Found: N, 4·7%).

(d) *From 4-thionflavone methiodide.* Benzylamine (5 drops) was added to a suspension of 4-thionflavone methiodide (100 mg.; see following paper) in ethanol (5 c.c.). Methanethiol was

evolved and the red colour of the methiodide disappeared almost immediately. After the mixture had been kept for 15 minutes at room temperature, water was added and the crystalline flavone benzylimine was collected (58 mg., 71%); after crystallisation it had m. p. and mixed m. p. 95—96°.

Flavone benzylimine picrate, prepared by mixing ethanolic solutions of either flavone benzylimine or 2-hydroxyflavanone benzylimine (VII) and of picric acid, forms a yellow powder, m. p. 242° (decomp.), insoluble in most organic solvents (Found: C, 62·2; H, 3·5; N, 10·4. $C_{22}H_{17}ON,C_6H_3O_7N_3$ requires C, 62·2; H, 3·7; N, 10·4%). *Flavone benzylimine hydrochloride* (63 mg., 88%), m. p. 270° (decomp.), was formed when concentrated hydrochloric acid was added to a solution of flavone benzylimine (64 mg.) in 10% acetic acid (10 c.c.); it could not be recrystallised (Found: N, 3·3; Cl, 9·2. $C_{22}H_{17}ON,HCl$ requires N, 4·0; Cl, 10·2%).

Flavone benzylimine was recovered as its hydrochloride after being heated under reflux for 4 hours with concentrated hydrochloric acid and sufficient glacial acetic acid to dissolve it.

Reaction of Hydrogen Sulphide with Flavone Benzylimine (IX).—Hydrogen sulphide was passed at room temperature into a solution of flavone benzylimine (0·5 g.) in ethanol (15 c.c.) for ½ hour. 4-Thionflavone rapidly separated from the red solution and was collected after 2 hours, washed with water, and dried (yield 0·277 g., 72%; m. p. 87°). Crystallisation from light petroleum (b. p. 60—80°) gave the pure compound, m. p. and mixed m. p. 88°.

Flavone Benzylimine Methiodide (X) *and its Hydrolysis*.—Flavone benzylimine (760 mg.) and methyl iodide (10 c.c.) in methanol (10 c.c.) were heated for 6 hours, the methanol removed, and the solid which separated was collected, washed with ether, and dried, giving *flavone benzylimine methiodide* (576 mg., 52%) as minute, yellow crystals, m. p. 266° (decomp. after darkening at 258°). This methiodide was also obtained by boiling 2-hydroxyflavanone benzylimine (VII) with methanolic methyl iodide (Found: C, 60·3; H, 4·2; N, 3·3; I, 28·8. $C_{22}H_{17}ON,CH_3I$ requires C, 60·9; H, 4·5; N, 3·1; I, 28·0%). Flavone benzylimine methiodide (1·39 g.), ethanol (100 c.c.), and water (100 c.c.) containing 2N-sodium hydroxide (1·6 c.c., 1 equiv.) were heated under reflux for 48 hours. Concentrated hydrochloric acid (10 c.c.) was added, and the ethanol removed under reduced pressure. Flavone (590 mg., 87%), m. p. and mixed m. p. 96—97°, was collected, and the filtrate was evaporated under reduced pressure, the residue dissolved in a small volume of hot ethanol and filtered, and ether added. Colourless plates of benzylamine hydrochloride (271 mg., 61%) separated, m. p. and mixed m. p. 256—258°; on admixture with *N*-methylbenzylamine hydrochloride (m. p. 177—179°) it melted at *ca.* 140—150°. *N*-Methylbenzylamine hydrochloride was recovered unchanged when it replaced the flavone benzylimine methiodide in the above experiment.

2-*Hydroxyflavanone* n-*Butylimine*.—A mixture of *o*-hydroxydibenzoylmethane (5 g.), *n*-butylamine (1·53 g.), and methanol (100 c.c.) was heated for 3 hours and concentrated to 50 c.c., and water added. The precipitate (2·23 g., 36%) was crystallised from methanol, giving 2-*hydroxyflavanone* n-*butylimine* as colourless prisms, m. p. 148° (decomp.) (Found: C, 76·9; H, 7·1; N, 4·8. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·2; N, 4·7%)

Flavone n-*Butylimine*.—(*a*) 2-Hydroxyflavanone *n*-butylimine (114 mg.) was heated on a steam-bath with glacial acetic acid (3·5 c.c.) for 10 minutes, cooled, poured into water, and neutralised with aqueous sodium carbonate. The precipitate of *flavone* n-*butylimine* (98 mg., 91%) separated from aqueous methanol as colourless platelets, m. p. 44—45° (Found: C, 82·4; H, 7·1; N, 5·0. $C_{19}H_{19}ON$ requires C, 82·3; H, 6·9; N, 5·0%).

(*b*) 4-Thionflavone (150 mg.), *n*-butylamine (0·5 c.c.), and methanol (10 c.c.) were heated for 1·5 hours and cooled; water was added until the solution was slightly cloudy, and the latter was placed in a refrigerator. The solid (117 mg., 67%) was collected and crystallised from aqueous methanol, giving flavone *n*-butylimine, m. p. and mixed m. p. 44—45°.

2-*Hydroxyflavanone* n-*Octylimine*.—As in the previous case, *o*-hydroxydibenzoylmethane (2·5 g.), *n*-octylamine (2 c.c.), and ethanol (25 c.c.) gave 2-*hydroxyflavanone* n-*octylimine* (3 g., 82%) as colourless plates, m. p. 110°, from light petroleum (b. p. 60—80°) or from aqueous ethanol (Found: C, 78·1; H, 8·5; N, 3·9. $C_{23}H_{29}O_2N$ requires C, 78·6; H, 8·3; N, 4·0%).

Flavone n-*Octylimine*.—(*a*) 2-Hydroxyflavanone *n*-octylimine (400 mg.) in acetic acid (4 c.c.) gave *flavone* n-*octylimine* (300 mg., 80%) as colourless, silky needles, m. p. 51—53°, from aqueous methanol (Found: C, 82·5; H, 7·8; N, 4·2. $C_{23}H_{27}ON$ requires C, 82·9; H, 7·8; N, 4·2%).

(*b*) 4-Thionflavone (100 mg.) and *n*-octylamine (0·5 c.c.) in ethanol (10 c.c.) gave, as in the previous case, flavone *n*-octylimine (101 mg., 72%), m. p. and mixed m. p. 51—53°. When treated in alcoholic solution with hydrogen sulphide (as described in the case of flavone benzylimine) it gave 4-thionflavone in 91% yield.

o-Hydroxyacetophenone Benzylimine (XII).—Benzylamine (1·96 g.) was added to *o*-hydroxy-

acetophenone (2·3 g.) in ethanol (10 c.c.). Heat was evolved and the precipitate (3·34 g., 88%) which separated on cooling was collected and crystallised from ethanol, giving *o-hydroxyacetophenone benzylimine* as pale green needles, m. p. 117·5—118·5° (Found: C, 80·0; H, 6·8; N, 6·2. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%). This compound shows an intense blue-green fluorescence in ultra-violet light, gives a wine-red ferric chloride reaction, and is insoluble in dilute alkali. It dissolves in dilute acid with loss of colour, and the odour of *o*-hydroxyacetophenone is apparent. With cupric acetate it gave a *copper* derivative, which separated from a large volume of ethanol as intensely dark-green prisms, m. p. 194—196° [Found: C, 70·0; H, 5·2; N, 5·4; Cu, 12·4. $(C_{15}H_{14}ON)_2Cu$ requires C, 70·4; H, 5·5; N, 5·5; Cu, 12·4%].

2-β-n-*Hexylaminocrotonoylphenol.*—*n*-Hexylamine (1·1 mol.) was added to a solution of 2-acetoacetylphenol (1 mol.) in ethanol at room temperature. The resulting yellow, fluorescent solution deposited bright yellow crystals which were collected after 2 days and recrystallised from ethanol (yield, 67%). This 2-β-n-*hexylaminocrotonoylphenol* has m. p. 95—96° (Found: C, 73·3; H, 8·8; N, 5·6. $C_{16}H_{23}O_2N$ requires C, 73·6; H, 8·8; N, 5·4%). The *copper* derivative separated in almost quantitative yield when ethanolic solutions of 2-β-*n*-hexylaminocrotonoylphenol and of cupric acetate were mixed. After recrystallisation from a large volume of benzene it formed a mass of thread-like, green needles, m. p. 270° [Found: C, 59·8; H, 6·6; N, 4·3; Cu, 19·8. $(C_{16}H_{21}O_2NCu)_n$ requires C, 59·5; H, 6·5; N, 4·3; Cu, 19·7%].

Copper Derivatives of 2-β-*Benzylamino-crotonoyl- and -cinnamoyl-phenol.*—The first *copper* derivative was prepared as in the previous case, and obtained in green, thread-like needles from dioxan, m. p. 278° [Found: C, 62·45; H, 4·5; N, 4·2; Cu, 18·2. $(C_{17}H_{15}O_2NCu)_n$ requires C, 62·1; H, 4·6; N, 4·25; Cu, 19·3%]; the second *copper* derivative separated from pyridine–ethanol as a dark green powder, m. p. 312° (decomp.) [Found: C, 68·3; H, 4·7; N, 3·5; Cu, 18·0. $(C_{22}H_{17}O_2NCu)_n$ requires C, 67·6; H, 4·4; N, 3·6; Cu, 16·3%].

Reaction of Benzylamine with o-*Hydroxy*-p′-*methoxydibenzoylmethane* (XIII; R = OMe). 2-*Hydroxy*-4′-*methoxyflavanone Benzylimine.*—The diketone (XIII; R = OMe) (1 g.), benzylamine (0·45 c.c.), and methanol (30 c.c.) were heated for 3 hours, and the solution was concentrated and cooled. The solid (0·87 g., 65%) was collected (the mother-liquors were not fluorescent), dried, and recrystallised from aqueous methanol (charcoal), giving 2-*hydroxy*-4′-*methoxyflavanone benzylimine* as colourless plates, m. p. 160° (decomp.) (Found: C, 76·5; H, 5·6; N, 4·2. $C_{23}H_{21}O_3N$ requires C, 76·9; H, 5·9; N, 3·9%).

4′-*Methoxyflavone Benzylimine.*—2-Hydroxy-4′-methoxyflavanone benzylimine (95 mg.) and glacial acetic acid (3 c.c.) were heated on a steam-bath for 10 minutes and poured into aqueous sodium carbonate. The solid (74 mg., 82%) was collected, washed, dried, and crystallised from ethanol, giving 4′-*methoxyflavone benzylimine* as long, colourless needles, m. p. 134—135° (Found: C, 80·9; H, 5·5; N, 4·0. $C_{23}H_{19}O_2N$ requires C, 80·9; H, 5·6; N, 4·1%). Its solution in ethanol shows a vivid blue fluorescence in ultra-violet light. With ethanolic picric acid it gave a *picrate* as a yellow powder, m. p. 252° (decomp.) (Found: C, 61·2; H, 3·9; N, 9·6. $C_{23}H_{19}O_2N,C_6H_3O_7N_3$ requires C, 61·1; H, 3·9; N, 9·8%).

o-(p-*Chlorobenzoyloxy*)*acetophenone.*—A mixture of *p*-chlorobenzoyl chloride (13·8 g.), *o*-hydroxyacetophenone (10·7 g.), and dry pyridine (30 c.c.) was kept overnight and poured into dilute hydrochloric acid and ice. The solid was collected, washed, dried, and crystallised from ethanol, giving o-(p-*chlorobenzoyloxy*)*acetophenone* (17·3 g., 81%) as colourless plates, m. p. 92—93° (Found: C, 65·4; H, 4·2; Cl, 12·5. $C_{15}H_{11}O_3Cl$ requires C, 65·6; H, 4·0; Cl, 12·9%).

p-*Chloro*-o′-*hydroxydibenzoylmethane* (XIII; R = Cl).—The preceding ester (20 g.) in dry pyridine (200 c.c.) was mechanically stirred and treated at room temperature with powdered potassium hydroxide (5 g.). After 3 hours, the mixture was poured into dilute acetic acid and ice, and the solid collected, washed, dried, and recrystallised from ethanol, giving p-*chloro*-o′-*hydroxydibenzoylmethane* (12·15 g., 61%) as fine, yellow needles, m. p. 122—124° (Found: C, 65·6; H, 4·1; Cl, 14·0. $C_{15}H_{11}O_3Cl$ requires C, 65·6; H, 4·0; Cl, 12·9%). It gave an intense wine-red colour with ferric chloride.

4′-*Chloroflavone.*—The preceding diketone (500 mg.), acetic acid (5 c.c.), and concentrated hydrochloric acid (5 drops) were heated on a steam-bath for 15 minutes and poured into water, and the solid (430 mg., 92%) was collected, dried, and crystallised from ethanol, giving 4′-*chloroflavone* as long, colourless needles, m. p. 188—189° (Found: C, 70·2; H, 3·5; Cl, 14·1. $C_{15}H_9O_2Cl$ requires C, 70·2; H, 3·5; Cl, 13·8%).

Reaction of Benzylamine with p-*Chloro*-o′-*hydroxydibenzoylmethane* (XIII; R = Cl). 4′-*Chloro*-2-*hydroxyflavanone Benzylimine.*—As in the previous case, the solid (4·45 g., 84%), obtained after heating the diketone (XIII; R = Cl) (4 g.) with benzylamine (4 c.c.) in ethanol

(100 c.c.) for 7 hours, was crystallised from aqueous methanol (charcoal) and then from benzene, giving *4'-chloro-2-hydroxyflavanone benzylimine* as microscopic, colourless plates, m. p. 158° (decomp.) (Found: C, 72·2; H, 4·8; N, 3·7; Cl, 11·7. $C_{22}H_{18}O_2NCl$ requires C, 72·6; H, 4·95; N, 3·95; Cl, 9·8%). The original mother-liquors were fluorescent but the substance responsible was present only in traces.

4'-Chloroflavone Benzylimine.—The above benzylamine derivative (500 mg.) was cyclised by warming it with glacial acetic acid (5 c.c.) in the usual way and gave *4'-chloroflavone benzylimine* (360 mg., 76%), which separated from aqueous ethanol as fine, colourless needles, m. p. 131° (Found: C, 75·7; H, 4·5; N, 4·3; Cl, 10·4. $C_{22}H_{16}ONCl$ requires C, 76·4; H, 4·6; N, 4·1; Cl, 10·3%). It was characterised as its *picrate*, a yellow powder, m. p. 250° (decomp.) (Found: C, 58·3; H, 3·4; N, 9·8; Cl, 6·2. $C_{22}H_{16}ONCl, C_6H_3O_7N_3$ requires C, 58·5; H, 3·3; N, 9·8; Cl, 6·2%).

o-*Hydroxy*-p'-*nitrodibenzoylmethane* (XIII; R = NO_2).—*o*-(*p*-Nitrobenzoyloxy)acetophenone (Doyle, Gógan, Gowan, Keane, and Wheeler, *Proc. Roy. Dublin Soc.*, 1948, **24**, 304) (6·7 g.) in dry pyridine (100 c.c.) was stirred at room temperature with powdered potassium hydroxide (1·7 g.). After 3 hours the mixture was poured on dilute hydrochloric acid and ice, and the crude diketone was collected, washed, dried (5·43 g., 81%), and crystallised from benzene, giving *o*-hydroxy-*p'*-nitrodibenzoylmethane (3·74 g., 56%) as deep yellow prisms, m. p. 200—201°. Doyle *et al.* (*loc. cit.*) rearranged the ester in presence of ethyl sodioacetoacetate and obtained a 47% yield of crude diketone; they recorded m. p. 198—201°.

Reaction of Benzylamine with o-*Hydroxy*-p'-*nitrodibenzoylmethane* (XIII; R = NO_2). *Formation of* o-*Hydroxyacetophenone Benzylimine* (XII), *Methyl* p-*Nitrobenzoate, and* 4'-*Nitroflavone.*—(a) The diketone (1·47 g.), benzylamine (0·6 c.c.), and methanol (200 c.c.) were heated for 2·5 hours, the solvent was removed under diminished pressure, and the residue triturated with benzene. The insoluble material (0·11 g., 8%) crystallised from acetic acid and then from acetone, giving 4'-nitroflavone, as colourless needles, m. p. 237—239°, undepressed when mixed with an authentic specimen (Doyle *et al.*, *loc. cit.*, give m. p. 236°). Light petroleum (b. p. 60—80°) was added to the benzene filtrate, and the solid (0·6 g.; 52%) which separated on cooling was crystallised from aqueous methanol, giving *o*-hydroxyacetophenone benzylimine, m. p. and mixed m. p. 117·5—118·5°.

(*b*) In another experiment, the diketone (1 g.) and benzylamine (0·85 c.c.) in methanol (100 c.c.) were heated for 1·75 hours, then cooled, and 2N-sulphuric acid (100 c.c.) added to hydrolyse the *o*-hydroxyacetophenone benzylimine. The precipitate (107 mg., 11%) was collected and identified as 4'-nitroflavone. The filtrate was diluted with water and neutralised with 2N-sodium hydroxide, and the precipitate (0·32 g., 36%) which separated was collected and crystallised from ethanol, giving methyl *p*-nitrobenzoate, m. p. and mixed m. p. with an authentic specimen, 95—96° (Wilbrand and Beilstein, *Annalen*, 1863, **128**, 263).

2-*Hydroxy*-4 : 6-*dimethoxydibenzoylmethane.*—Powdered potassium hydroxide (1·6 g.) was added to 2-benzoyloxy-4 : 6-dimethoxyacetophenone (7 g.; Gulati and Venkataraman, *J.*, 1936, 267) in dry pyridine (35 c.c.) and, after being shaken overnight at room temperature, the mixture was poured into dilute hydrochloric acid and ice. The product solidified on storage and was recrystallised from ethanol (charcoal), giving *2-hydroxy-4 : 6-dimethoxydibenzoylmethane* (1·78 g., 26%) as colourless prisms, m. p. 128—130° (Found: C, 68·3; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·3%). This compound was described by Gulati and Venkataraman (*loc. cit.*) as an oil. It gave an intense green ferric chloride colour. It was recovered unchanged after treatment with benzylamine in boiling alcoholic solution.

5 : 7-*Dimethoxyflavone.*—The above diketone (100 mg.) in glacial acetic acid (2·5 c.c.) with concentrated hydrochloric acid (1 drop) gave, in the usual way, 5 : 7-dimethoxyflavone (60 mg., 64%), m. p. 143—145° after drying under diminished pressure over phosphoric anhydride (Gulati and Venkataraman, *loc. cit.*, give m. p. 143°).

2-2'-*Furyl*-2-*hydroxychromanone Benzylimine.*—2-Furoyl-*o*-hydroxybenzoylmethane (XIV) (3·85 g.; Baker, Ollis, and Weight, forthcoming publication) and benzylamine in ethanol (100 c.c.) gave in the usual way *2-2'-furyl-2-hydroxychromanone benzylimine* (2·75 g., 51%) as colourless plates, m. p. 158—159° (decomp.), from ethanol (charcoal) (Found: C, 74·7; H, 5·3; N, 4·3. $C_{20}H_{17}O_3N$ requires C, 75·2; H, 5·3; N, 4·4%).

2-2'-*Furylchromone Benzylimine* (XV).—The preceding hydroxychromanone was warmed with glacial acetic acid and gave as in previous cases *2-2'-furylchromone benzylimine* (72% yield) as colourless, silky needles, m. p. 120—122°, from ethanol (Found: C, 79·7; H, 5·2; N, 4·6. $C_{20}H_{15}O_2N$ requires C, 79·7; H, 5·0; N, 4·65%).

3-2'-*Furoyl*-2-*methylchromone.*—2-Furoyl-*o*-hydroxybenzoylmethane (XIV) (1 g.), acetic anhydride (5 c.c.), and anhydrous sodium acetate (1 g.) were heated at 150—160° for 20 minutes,

cooled, and poured into water. The solid was collected, washed, dried, and crystallised from aqueous methanol, giving 3-2′-*furoyl*-2-*methylchromone* (0·62 g., 56%) as colourless needles, m. p. 148—150° (Found: C, 70·4; H, 3·9. $C_{15}H_{10}O_4$ requires C, 70·9; H, 3·9%).

Reaction of Benzylamine with 3-2′-*Furoyl*-2-*methylchromone. Formation of* 2-β-*Benzylaminocrotonoylphenol.*—The chromone (0·4 g.), benzylamine (0·4 c.c.), and ethanol (10 c.c.) were heated for 2 hours, and the solution was concentrated. The solid (0·22 g.) was collected and crystallised from ethanol, giving 2-β-benzylaminocrotonoylphenol, m. p. and mixed m. p. 123—124°.

Action of Acetic Anhydride on o-*Hydroxy*-p′-*nitrodibenzoylmethane* (XIII; R = NO_2). *Formation of* 2-*Methyl*-3-p-*nitrobenzoylchromone.*—o-Hydroxy-*p*′-nitrodibenzoylmethane (1 g.), acetic anhydride (5 c.c.), and anhydrous sodium acetate (1 g.) were heated for 15 minutes, cooled, and poured into water. The solid (1·03 g., 96%) was washed, dried, and crystallised from ethanol, giving 2-*methyl*-3-p-*nitrobenzoylchromone* as colourless needles, m. p. 202—204° (Found: C, 66·1; H, 3·8; N, 4·7. $C_{17}H_{11}O_5N$ requires C, 66·0; H, 3·6; N, 4·5%).

This chromone (0·5 g.) and benzylamine (0·4 c.c.) in pyridine (5 c.c.) were heated on a steam-bath for 2·5 hours, boiled for ¾ hour, and poured into dilute hydrochloric acid. The precipitate was crystallised from ethanol, giving 2-β-benzylaminocrotonoylphenol (0·26 g., 61%), m. p. and mixed m. p. 123—124°. Water was added to the mother-liquors and the solid (0·41 g., 100%) was crystallised from aqueous ethanol and then from benzene–light petroleum (b. p. 60—80°), giving *N*-benzyl-*p*-nitrobenzamide, m. p. and mixed m. p. 141—143°.

Reaction of Benzoic Anhydride with 2-*Acetoacetylphenol. Formation of* 3-*Benzoyl*-2-*methylchromone.*—2-Acetoacetylphenol (1 g.), benzoic anhydride (5 g.), and triethylamine (5 c.c.) were heated at 160° for 4 hours, water (40 c.c.) was added, and the mixture was heated for 2 hours. The cooled product was triturated with 2N-sodium carbonate, and the solid washed with water, dried, and crystallised from ethanol, giving 3-benzoyl-2-methylchromone (644 mg., 44%), m. p. and mixed m. p. with an authentic specimen, 117° (cf. Müller, *J.*, 1915, **107**, 872, who gives m. p. 118°).

" 3 : 3′-*Dianisoyl*-4 : 4′-*dimethoxydiflavone* " (XVII).—This compound was prepared in 18% yield by the method of Algar, McCarthy, and Dick (*loc. cit.*), but the product was difficult to purify and was erroneously given structure (XVI). The following method gave a 36% yield.

Anisic anhydride (25 g.), 4 : 6-diacetylresorcinol (2·5 g.), and triethylamine (10 c.c.) were stirred for 7 hours at 160°, poured into 5% aqueous sodium carbonate (300 c.c.), and heated for 2 hours. The solid which separated on cooling was crystallised from chloroform–ethanol, giving a pale brown powder (6·23 g., 70%), m. p. 218—225°, which after recrystallisation from glacial acetic acid gave " 3 : 3′-dianisoyl-4 : 4′-dimethoxydiflavone " [5′ : 5″-*dianisoyl*-6′ : 6″-*di*-p-*methoxyphenyldipyrono*(2′ : 3′-1 : 2)(3″ : 2″-4 : 5)*benzene*] (XVII) (3·25 g.) as colourless needles, m. p. 233—235° [Found: C, 72·3; H, 4·4; OMe, 17·1. $C_{38}H_{18}O_6(OMe)_4$ requires C, 72·6; H, 4·3; OMe, 17·9%]. This m. p. was undepressed when the specimen was mixed with the material prepared according to Algar, McCarthy, and Dick, who obtained pale yellow needles, m. p. 233—235°.

4 : 6-*Di*-(β-*benzylamino*-4-*methoxycinnamoyl*)*resorcinol* (XVIII).—The preceding compound (1 g.) and benzylamine (0·66 c.c.) in dry pyridine (25 c.c.) were heated for 16 hours and poured into dilute hydrochloric acid, and the solid collected, dried, and crystallised from benzene (yield 0·5 g.; 55%) and then from chloroform–ethanol. The *compound* (XVIII) formed short, yellow prisms, m. p. 200° (Found: C, 75·2; H, 5·6; N, 4·3; OMe, 9·4. $C_{40}H_{36}O_6N_2$ requires C, 75·0; H, 5·6; N, 4·4; OMe, 9·7%). It showed a vivid yellow fluorescence in ultra-violet light.

Addition of light petroleum (b. p. 60—80°) to the mother-liquors from the first benzene crystallisation gave *N*-benzyl-*p*-methoxybenzamide as a solid which separated from aqueous ethanol as colourless needles (0·30 g., 43%), m. p. and mixed m. p. with an authentic specimen, 131° (Beckmann, *Ber.*, 1904, **37**, 4138, gives m. p. 131°).

" 4 : 4′-*Dimethoxydiflavone* " (XIX).—The preceding dibenzylamino-derivative (100 mg.), glacial acetic acid (5 c.c.), and concentrated hydrochloric acid (5 drops) were heated on a steam-bath for 1 hour, during which time colourless needles separated. After cooling, this precipitate was collected and crystallised from chloroform-ethanol, giving " 4 : 4′-dimethoxydiflavone " [6′ : 6″-*di*-p-*methoxyphenyldipyrono*(2′ : 3′-1 : 2)(3″ : 2″-4 : 5)*benzene*] (XIX) (40 mg., 60%) as colourless needles, m. p. 320—322° (Algar *et al.*, *loc. cit.*, give m. p. 321—322°).

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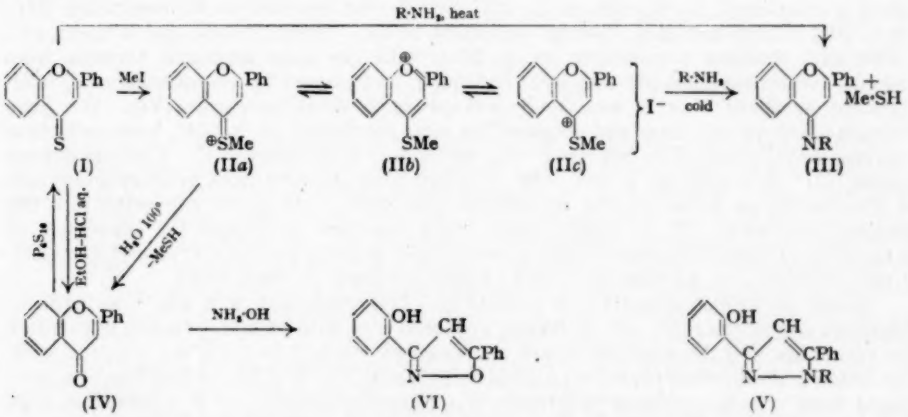
235. *Some Properties of 4-Thionflavone and its Methiodide, and of 4-Thionchromones.*

By WILSON BAKER, J. B. HARBORNE, and W. D. OLLIS

4-Thionflavone, prepared from flavone and phosphorus pentasulphide, is slowly hydrolysed by acids to flavone, and reacts with hydroxylamine on heating to give flavone oxime. 4-Thionflavone methiodide is much more reactive; it is hydrolysed by water to flavone, and gives at room temperature with the appropriate reagents, derivatives of flavone imine, including flavone oxime, hydrazone, and semicarbazone. The previously described " flavone oxime," prepared from flavone, is shown to be an *iso*oxazole, and " phenylhydrazones " derived from some 4-thionchromones are proved to be pyrazoles.

4-THIONFLAVONE (I), deep red needles, m. p. 87°, has been little studied, and was first prepared by Schnell (Diss., Berlin, 1921; the method was later published by Schönberg and Nickel, *Ber.*, 1931, **64**, 2325, and by Diesbach and Kramer, *Helv. Chim. Acta*, 1945, **28**, 1404) by heating flavone (IV) with phosphorus pentasulphide. By using purified phosphorus pentasulphide and toluene as solvent at 100°, 4-thionflavone is now readily prepared in 55% yield. Its structure follows from the facts that it differs from 1-thiaflavone (prepared by cyclisation of β-phenylthiocinnamic acid, Ruhemann, *Ber.*, 1913, **46**, 2197), that it shows no phenolic properties, and that it is extremely easily reconverted into flavone by hydrolysis of its methiodide (see p. 1306).



4-Thionflavone is unaffected by hot methanolic barium hydroxide, which converts flavone into *o*-hydroxydibenzoylmethane (Müller, *J.*, 1915, **107**, 872). It is, however, slowly hydrolysed to flavone and hydrogen sulphide by boiling ethanolic hydrochloric acid. It very readily forms a dark, maroon-coloured methiodide, which undoubtedly contains a mesomeric cation derived from canonical forms such as (II*a*), (II*b*), and (II*c*).

4-Thionflavone methiodide (II) is extremely reactive; it is hydrolysed rapidly by boiling water, giving flavone (IV) and methanethiol, and quickly reacts at room temperature with many compounds containing the anionoid amino-group to form methanethiol and derivatives of flavone imine. Form (II*c*) is doubtless the reactive form of the molecule involved in attack by these anionoid reagents. Thus, with the appropriate reagents, it yields flavone benzylimine (III; R = CH_2Ph) (preceding paper), flavone anil (III; R = Ph), flavone hydrazone (III; R = NH_2), flavone benzoylhydrazone (III; R = NH·COPh), flavone semicarbazone (III; R = NH·CO·NH_2), flavone thionsemicarbazone (III; R = NH·CS·NH_2), and flavone oxime (III; R = OH). The flavone hydrazone (III; R = NH_2)

gave an *N*-benzoyl derivative, identical with the product prepared from 4-thionflavone methiodide (II) and benzoylhydrazine, an *N*-acetyl derivative (III; R = NHAc), and a benzylidenehydrazine derivative (III; R = N:CHPh). None of the above compounds containing –N–N– groups shows phenolic properties, and they are, therefore, correctly represented as flavone hydrazones, and not as the isomeric, phenolic pyrazoles (V; R = H, COPh, $CO{\cdot}NH_2$, and $CS{\cdot}NH_2$), one of which (V; R = H) has for comparison been prepared from *o*-hydroxydibenzoylmethane and hydrazine. In addition, flavone hydrazone reacts with a further molecule of 4-thionflavone methiodide to give 4-flavyleneazine; attempts to convert the latter compound into di-4-flavylene by loss of nitrogen were unsuccessful.

It was shown in the preceding paper that the reaction of 4-thionflavone with benzylamine to give flavone benzylimine is reversible, since the benzylimine with excess of hydrogen sulphide in boiling ethanol gave 4-thionflavone. Under the same conditions only a trace of 4-thionflavone is formed from flavone anil, and flavone oxime and flavone phenylhydrazone are unaffected. Flavone hydrazone and hydrogen sulphide gave some 4-flavyleneazine, which must result from interaction of flavone hydrazone and 4-thionflavone.

4-Thionflavone, as might be expected, is much less reactive towards anionoid reagents than its methiodide. It is not affected by boiling water, and reacts only on heating with hydroxylamine (this paper), benzylamine, *n*-butylamine, and *n*-octylamine (preceding paper), to give derivatives of flavone imine (III); it does not react with aniline even on prolonged boiling. It is nevertheless appreciably more reactive towards carbonyl reagents than is flavone, which is as yet known to yield directly only a 2 : 4-dinitrophenylhydrazone. In view of possible alternative, isomeric structures for this compound, for " flavone oxime," and for flavone phenylhydrazone, some comment is desirable.

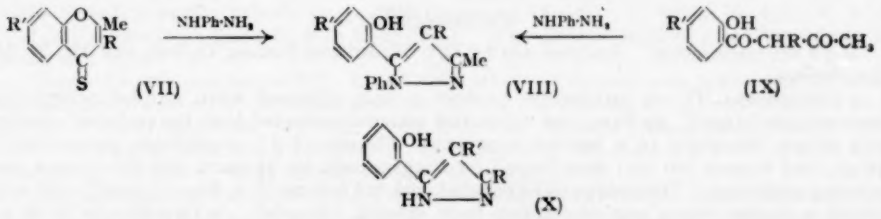
Flavone oxime. Reaction of flavone with hydroxylamine hydrochloride in pyridine gives a compound, $C_{15}H_{11}O_2N$, m. p. 237°, which was regarded as flavone oxime (III; R = OH) (Gulati and Ray, *Current Sci.*, 1936, **5**, 75). Shenoi, Shah, and Wheeler, (*J.*, 1940, 247) obtained a substance, m. p. 231°, with the same molecular formula from *o*-hydroxydibenzoylmethane and hydroxylamine, and proved by an unambiguous, independent synthesis that it was 3-*o*-hydroxyphenyl-5-phenyl*iso*oxazole (VI). We have repeated both preparations and obtained the same compound, m. p. 234°, from each, thus proving that the previously described " flavone oxime " is in reality (VI). The true flavone oxime (III; R = OH), m. p. 184—186°, has now been prepared from hydroxylamine and 4-thionflavone or 4-thionflavone methiodide (see above). It is not converted into the isomeric *iso*oxazole (VI) by boiling alkali, being recovered unchanged [cf. conversion of 2-methyl-3-(1-phenylhydrazonoethyl)chromone into 4-acetyl-5-*o*-hydroxyphenyl-3-methyl-1-phenylpyrazole by reaction with alkali; Baker and Butt, *J.*, 1949, 2150].

Flavone phenylhydrazone (III; R = NHPh). This compound, m. p. 155°, was made by Diesbach and Kramer (*loc. cit.*) by boiling 4-thionflavone with phenylhydrazine in pyridine for two hours, and the structure is now confirmed by the fact that it is not identical with the isomeric 3-*o*-hydroxyphenyl-1 : 5-diphenylpyrazole (V; R = Ph), which has been prepared from *o*-hydroxydibenzoylmethane and phenylhydrazine. It is assumed in this latter reaction that the phenylhydrazine reacts with the carbonyl group attached to the phenolic nucleus as do benzylamine (previous paper) and hydroxylamine (Shenoi, Shah, and Wheeler, *loc. cit.*). Flavone phenylhydrazone is not isomerised to the pyrazole (V; R = Ph) by heating it with alkali.

Flavone 2 : 4-*dinitrophenylhydrazone* [III; R = $NH{\cdot}C_6H_3(NO_2)_2$]. Adkins and Mozingo (*J. Amer. Chem. Soc.*, 1938, **60**, 675) prepared a substance, m. p. 282°, from flavone and 2 : 4-dinitrophenylhydrazine in alcoholic sulphuric acid, and assumed that it was flavone 2 : 4-dinitrophenylhydrazone because it differed from a compound (not analysed), m. p. 119—120°, similarly prepared from *o*-hydroxydibenzoylmethane. In attempting to repeat the latter reaction, we isolated only a 2 : 4-dinitrophenylhydrazone, m. p. 282°, identical with that prepared from flavone, but we would note, in connection with the claim of Adkins and Mozingo, that *o*-hydroxydibenzoylmethane has m. p. 120—122°, and that it is converted into flavone by heating it with acids in alcoholic solution. The possibility remained, therefore, that the derivative, m. p. 282°, might be a pyrazole [V; R = $C_6H_3(NO_2)_2$], but the fact that the same substance has now been prepared in high yield at room temperature

from 4-thionflavone methiodide and 2 : 4-dinitrophenylhydrazine in alcoholic sulphuric acid, suffices to establish the structure as that of flavone 2 : 4-dinitrophenylhydrazone. The unique carbonyl reactivity of flavone thus disclosed may be ascribed to its probable conversion into the oxonium cation by acceptance of a proton from the ethanolic sulphuric acid; this cation, like the cation of 4-thionflavone methiodide, would be expected to be readily attacked by anionoid reagents.

"Phenylhydrazones" of some 2-methyl-4-thionchromones. Simonis and Rosenberg (*Ber.*, 1914, **47**, 1232) prepared 2 : 3-dimethyl- and 2 : 3 : 5- and 2 : 3 : 8-trimethyl-4-thionchromones and treated them with phenylhydrazine in presence of alkali, obtaining yellow products regarded as the chromone phenylhydrazones. There was reason to doubt, however, whether these reactions had been correctly interpreted, since Baker and Butt (*J.*, 1949, 2147) showed that 7-methoxy-2-methyl-4-thionchromone (VII; R = H, R′ = OMe) reacted with phenylhydrazine and alkali to give the phenolic 5-(2-hydroxy-4-methoxyphenyl)-3-methyl-1-phenylpyrazole (VIII; R = H, R′ = OMe), a compound which was also prepared from phenylhydrazine and 2-acetoacetyl-5-methoxyphenol (IX; R = H, R′ = OMe). It has also been found (see p. 1308) that both 2-methyl-4-thionchromone (VII; R = R′ = H) and 2-acetoacetylphenol (IX; R = R′ = H) react with phenylhydrazine to give the colourless, phenolic 5-*o*-hydroxyphenyl-3-methyl-1-phenylpyrazole (VIII; R = R′ = H).



2 : 3-Dimethyl-4-thionchromone (VII; R = Me, R′ = H) and phenylhydrazine gave, as previously described by Simonis and Rosenberg, a product, m. p. 209°; it was, however, colourless and exhibited phenolic properties, giving an acetyl derivative. This substance is clearly 5-*o*-hydroxyphenyl-3 : 4-dimethyl-1-phenylpyrazole (VIII; R = Me, R′ = H), and it must be concluded that the other products described by Simonis and Rosenberg as chromone phenylhydrazones are in reality the isomeric pyrazoles. The mechanism of pyrazole formation from 2-methyl-4-thionchromones (VII) and phenylhydrazine in presence of aqueous-alcoholic alkali may involve as the first step or addition of phenylhydrazine to the 2 : 3-double bond of (VII) (cf. reaction of benzylamine with, *e.g.*, 3-acetyl-2-methylchromone under anhydrous conditions which proceeds by way of addition of the amine to the 2 : 3-double bond; Baker and Butt, *loc. cit.*, p. 2143).

These results are in harmony with the observation of Koenigs and Freund (*Ber.*, 1947, **80**, 146) that 2-methylchromone reacts with hydrazine hydrate to give 3(5)-*o*-hydroxyphenyl-5(3)-methylpyrazole (X; R = Me, R′ = H). This same pyrazole has now been obtained from hydrazine hydrate and 2-acetoacetylphenol (IX; R = R′ = H) or 2-methyl-4-thionchromone (VII; R = R′ = H), and in a similar manner 2 : 3-dimethyl-4-thionchromone (VII; R = Me, R′ = H) gave 3(5)-*o*-hydroxyphenyl-4 : 5(3 : 4)-dimethylpyrazole (X; R = R′ = Me).

Schönberg and Stolpp (*Ber.*, 1930, **63**, 3116) have shown that chromone and 4-thionchromone react with hydrazine to give the same product, m. p. 96°, which was regarded as chromone hydrazone. The reaction of chromone with hydrazine has been repeated, but the product is phenolic, being soluble in aqueous sodium hydroxide and giving a strong blue ferric chloride reaction, and it must, therefore, be 3(5)-*o*-hydroxyphenylpyrazole (X; R = R′ = H). This conclusion is supported by its ultra-violet absorption spectrum recorded below.

The ultra-violet absorption maxima ($\lambda_{max.}$ mμ) of the pyrazoles described in this paper

are given below. Measurements were made in ethanol, and the values of log $\varepsilon_{max.}$ are given in parentheses.

Pyrazole derivative	$\lambda_{max.}$ (log $\varepsilon_{max.}$)			
(1) 3(5)-*o*-Hydroxyphenyl-	215 (4·32);	248 (4·22);	258 (4·24);	293·5 (3·84)
(2) 3(5)-*o*-Hydroxyphenyl-5(3)-methyl-	211 (4·33);	248 (4·15);	259 (4·16);	294 (3·76)
(3) 3(5)-*o*-Hydroxyphenyl-4 : 5(3 : 4)-dimethyl- ...	211 (4·4);	252 (4·06);	262 (3·96);	292 (3·74)
(4) 3(5)-*o*-Hydroxyphenyl-5(3)-phenyl-	214 (4·58);	250 * (4·46);	256 (4·49);	294 (3·95)
(5) 5-*o*-Hydroxyphenyl-3-methyl-1-phenyl-	213 (4·39);		253 (4·15);	286 † (3·71)
				294 † (3·64)
(6) 5-*o*-Hydroxyphenyl-3 : 4-dimethyl-1-phenyl-	‡		258 (4·09);	No band
(7) 5-*o*-Hydroxyphenyl-2 : 3-diphenyl-	‡	250 (4·48);		296 (4·14)

* Inflexion. † Ill-defined maxima. ‡ Intense absorption, maxima probably at *ca.* 205.

The similarity of the spectra of the compounds (1)—(5) gives additional evidence that they are all of the same type and excludes the possibility that some are derivatives of chromone hydrazone, as has been previously suggested. The spectra of the compounds (1)—(4) show four maxima, and are more complicated than the other three, probably owing to prototropic tautomerism; the compounds (5)—(7) cannot be tautomeric. The band in the 290-mμ region is not shown for (6) and this may be due to steric interference of the phenolic group with the substituents in positions 1 and 4.

Experimental

M.p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

4-Thionflavone (I).—A satisfactory product is only obtained when purified phosphorus pentasulphide is used; we have used crystalline material extracted from the technical product with carbon disulphide in a Soxhlet apparatus. Flavone (5 g.), phosphorus pentasulphide (10 g.), and toluene (50 c.c.) were heated on a steam-bath for 3½ hours and the solvent was decanted whilst hot. The residue was extracted with hot toluene (3 × 20 c.c.), and the extracts yielded a residue which was crystallised from ethanol (charcoal). 4-Thionflavone (2·93 g., 55%) was obtained as deep red needles, m. p. 87° (lit., 87° and 89°).

Acid Hydrolysis of 4-Thionflavone.—4-Thionflavone (250 mg.) in ethanol (10 c.c.) and concentrated hydrochloric acid (1 c.c.) were heated on the steam-bath for 40 hours. Hydrogen sulphide was evolved and the deep red colour of the solution faded. The solution was evaporated under reduced pressure, and the residue crystallised twice from light petroleum (b. p. 60—80°), giving needles of flavone, m. p. and mixed m. p. 96—97° (yield, 65%).

4-Thionflavone Methiodide (II).—Methyl iodide (5 c.c.) was added to 4-thionflavone (300 mg.) in chloroform (15 c.c.), and after 18 hours the solid was collected and washed with acetone and ether. *4-Thionflavone methiodide* (460 mg., 96%) was obtained as fine, maroon-coloured needles, m. p. 220—222° (Found: C, 50·5; H, 3·6; S, 8·6; I, 33·1. $C_{16}H_{13}OSI$ requires C, 50·5; H, 3·4; S, 8·4; I, 33·4%).

Hydrolysis of 4-Thionflavone Methiodide.—The methiodide (100 mg.) was boiled with water (10 c.c.) for 10 minutes; dissolution then occurred and methanethiol was evolved. After cooling, the solid was collected and crystallised from light petroleum (b. p. 60—80°), giving flavone (54 mg., 92%), m. p. and mixed m. p. 96—97°.

Flavone Anil (III; R = Ph).—Aniline (1 c.c.) was shaken with a suspension of 4-thionflavone methiodide (250 mg.) in ethanol, and reaction was complete in 15 minutes. The *flavone anil* (160 mg., 82%), obtained on addition of water, separated from ethanol in deep yellow needles, m. p. 121·5—122·5° (Found: C, 84·9; H, 5·0; N, 4·6. $C_{21}H_{15}ON$ requires C, 84·9; H, 5·0; N, 4·7%). The *picrate* formed yellow needles, m. p. 230—240° (decomp.; dependent upon rate of heating) (Found: N, 10·4. $C_{21}H_{15}ON,C_6H_3O_7N_3$ requires N, 10·6%).

Flavone Hydrazone (III; R = NH_2).—Hydrazine hydrate (0·5 c.c.) was added to a solution of 4-thionflavone (200 mg.) in warm ethanol (10 c.c.). The deep red colour rapidly disappeared, hydrogen sulphide was evolved and, after 10 minutes, water was added. The solid (130 mg., 65%) which separated after some time in a refrigerator crystallised from aqueous methanol, giving *flavone hydrazone* as deep yellow needles, m. p. 136° (Found: C, 76·0; H, 5·1; N, 12·0. $C_{15}H_{12}ON_2$ requires C, 76·2; H, 5·1; N, 11·9%). It showed no phenolic properties. The *benzylidene* derivative (III; R = N:CHPh) separated when flavone hydrazone (100 mg.) and benzaldehyde (1 c.c.) in methanol (3 c.c.) were kept at room temperature overnight. The pre-

cipitate (113 mg., 83%) was collected and crystallised from ethanol, giving yellow needles, m. p. 136° (Found: C, 80·7; H, 4·8; N, 8·7. $C_{22}H_{16}ON_2$ requires C, 81·45; H, 4·9; N, 8·7%). The N-*acetyl* derivative (III; R = NHAc) was prepared from flavone hydrazone (100 mg.), acetic anhydride (5 c.c.), and pyridine (2 drops); after being kept at room temperature overnight, the mixture was poured into water, and the solid (112 mg., 96%) crystallised from dioxan, giving almost colourless needles, m. p. 284° (Found: C, 73·3; H, 5·4; N, 9·8. $C_{17}H_{14}O_2N_2$ requires C, 73·4; H, 5·0; N, 10·1%).

Flavone Benzoylhydrazone (III; R = NH·COPh).—(*a*) Benzoylhydrazine (72 mg.) was added to a suspension of 4-thionflavone methiodide (200 mg.) in ethanol (10 c.c.), and after 15 minutes' shaking (methanethiol was evolved), the yellow solid was collected. Crystallisation from ethanol gave *flavone benzoylhydrazone* (85 mg., 47%) as microscopic yellow crystals, m. p. 244° (decomp.) (Found: C, 77·5; H, 4·7; N, 8·35. $C_{22}H_{16}O_2N_2$ requires C, 77·6; H, 4·7; N, 8·2%).

(*b*) Benzoyl chloride (0·049 c.c.) was added to flavone hydrazone (100 mg.) in pyridine (1 c.c.) and after 2·5 hours the mixture was poured into dilute hydrochloric acid. The solid was collected (146 mg., 100%) and crystallised from ethanol (40 c.c.) and water (20 c.c.), giving flavone benzoylhydrazone, m. p. and mixed m. p. 244° (decomp.).

Flavone Semicarbazone (III; R = NH·CO·NH_2).—An aqueous solution of semicarbazide hydrochloride (1 g.) and sodium acetate (1 g.) was added to 4-thionflavone methiodide (200 mg.) suspended in ethanol. The reaction was complete after a few minutes' shaking, and the solid was collected (132 mg., 90%) and crystallised from ethanol (30 c.c.), giving *flavone semicarbazone* as bright yellow, irregular prisms, m. p. 245° (decomp.) (Found: C, 69·0; H, 4·7; N, 15·3. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·05%). It exhibited a brilliant green fluorescence in ultra-violet light.

Flavone Thionsemicarbazone (III; R = NH·CS·NH_2).—4-Thionflavone methiodide (300 mg.) was added to a solution of thionsemicarbazide (300 mg.) in ethanol (50 c.c.) and water (50 c.c.). *Flavone thionsemicarbazone* (226 mg., 97%) separated as deep yellow plates, m. p. 234° (decomp.), from aqueous ethanol (Found: C, 64·2, 63·9, 63·6; H, 4·8, 4·5, 4·7; N, 13·8; S, 11·1. $C_{16}H_{13}ON_3S$ requires C, 65·1; H, 4·4; N, 14·2; S, 10·9%).

Flavone Oxime (III; R = OH).—(*a*) 4-Thionflavone (220 mg.), hydroxylamine hydrochloride (220 mg.), and pyridine (4 c.c.) were heated on a steam-bath for 30 minutes; hydrogen sulphide was evolved. The very pale yellow solution was poured into water and the solid was crystallised from ethanol, giving *flavone oxime* (157 mg., 72%) as colourless needles, m. p. 184—186° (Found: C, 76·1; H, 4·8; N, 6·2. $C_{15}H_{11}O_2N$ requires C, 75·9; H, 4·7; N, 5·9%).

(*b*) 4-Thionflavone methiodide (120 mg.) suspended in pyridine (3 c.c.) was shaken with hydroxylamine hydrochloride (120 mg.); immediate reaction occurred with evolution of methanethiol. After 5 minutes, the colourless solution was poured into 10% aqueous acetic acid, and the solid was crystallised from ethanol, giving flavone oxime (54 mg., 73%), m. p. and mixed m. p. 184°.

This flavone oxime was recovered unchanged after being heated under reflux either for 1 hour with aqueous-alcoholic 2N-sodium hydroxide or overnight with methanolic barium hydroxide.

3(5)-o-Hydroxyphenyl-5(3)-phenylpyrazole (V; R = H).—*o*-Hydroxydibenzoylmethane (1·1 g.), hydrazine hydrate (1 c.c.), and ethanol (10 c.c.) were heated under reflux for 20 minutes and cooled, water was added, and the solid collected, washed, dried (1·05 g., 97%), and crystallised from ethanol. 3(5)-o-*Hydroxyphenyl*-5(3)-*phenylpyrazole* was obtained as hexagonal plates, m. p. 144° (Found: C, 76·0; H, 5·1; N, 11·7. $C_{15}H_{12}ON_2$ requires C, 76·2; H, 5·1; N, 11·9%). It dissolves in 2N-sodium hydroxide giving a sparingly soluble sodium salt, and gives a deep green colour with aqueous-alcoholic ferric chloride.

4-Flavyleneazine.—(*a*) Reaction of flavone hydrazone (100 mg.) with 4-thionflavone methiodide (161 mg.) in ethanol (5 c.c.) yielded after 1 hour at room temperature a product (182 mg., 100%) which was crystallised by dissolving it in cold pyridine and carefully adding water. *4-Flavyleneazine* separated in orange, microscopic needles, m. p. 298° (decomp.) (Found: C, 81·75; H, 4·7; N, 6·5. $C_{30}H_{20}O_2N_2$ requires C, 81·8; H, 4·6; N, 6·4%).

(*b*) Hydrogen sulphide was passed through a boiling solution of flavone hydrazone (100 mg.) in ethanol (10 c.c.) for 2 hours and, after cooling the solid was collected and crystallised from aqueous pyridine, giving 4-flavyleneazine (23 mg., 25%), m. p. and mixed m. p. 296° (decomp.).

3-o-Hydroxyphenyl-1:5-diphenylpyrazole (V; R = Ph).—*o*-Hydroxydibenzoylmethane (1 g.), phenylhydrazine (0·44 c.c.), and ethanol (10 c.c.) were heated under reflux for 2·5 hours, the solution concentrated to half its volume, and water added. The precipitate

(0·94 g., 72%) was crystallised from ethanol, giving 3-o-*hydroxyphenyl*-1 : 5-*diphenylpyrazole* as fine needles, m. p. 105—106° (Found : C, 80·5; H, 4·7; N, 8·5. $C_{21}H_{16}ON_2$ requires C, 80·8; H, 5·1; N, 9·0%).

Flavone 2 : 4-*Dinitrophenylhydrazone* [III; R = $NH{\cdot}C_6H_3(NO_2)_2$].—(*a*) Flavone and 2 : 4-dinitrophenylhydrazine gave, as described by Adkins and Mozingo (*loc. cit.*), a dark red powder, m. p. 282° (decomp.) after crystallisation from dioxan.

(*b*) 4-Thionflavone (0·5 g.) was added to a solution of 2 : 4-dinitrophenylhydrazine (1 g.) and concentrated sulphuric acid (2 c.c.) in ethanol (40 c.c.). After being heated to its b. p. (hydrogen sulphide evolved), the mixture was left overnight, giving a deep red precipitate (72 mg., 8%). Recrystallisation from dioxan gave flavone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 282° (decomp.).

(*c*) 4-Thionflavone methiodide (190 mg.), 2 : 4-dinitrophenylhydrazine (99 mg.), and concentrated sulphuric acid (3 drops) in ethanol (5 c.c.), were shaken at room temperature for 18 hours; methanethiol was evolved. The deep red powder (161 mg., 79%) was recrystallised from dioxan, giving flavone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 282° (decomp.) (Found : N, 14·2. Calc. for $C_{21}H_{14}O_5N_4$: N, 13·9%).

(*d*) By reaction of *o*-hydroxydibenzoylmethane with 2 : 4-dinitrophenylhydrazine according to method (*b*) (above), only flavone 2 : 4-dinitrophenylhydrazone was obtained, m. p. and mixed m. p. 282° (decomp.), in 18% yield (cf. Adkins and Mozingo).

2-*Methyl*-4-*thionchromone* (VII; R = R′ = H).—2-Methylchromone (2·5 g.), purified phosphorus pentasulphide (4·8 g.), and toluene (50 c.c.) were heated under reflux for 1·5 hours, the toluene was decanted whilst hot, and the residue was extracted with hot toluene (2 × 20 c.c.). The residue (2·0 g.) from the combined extracts was washed with hot ammonium sulphide solution, and crystallised from ethanol, giving 2-*methyl*-4-*thionchromone* (1·53 g., 56%) as very deep red needles, m. p. 96—97° (Found : C, 68·7; H, 4·8; S, 18·0. $C_{10}H_8OS$ requires C, 68·2; H, 4·5; S, 18·2%).

In another experiment, the 2-methyl-4-thionchromone was obtained as light red needles, m. p. 98° (Found : C, 68·3; H, 4·6; S, 18·5%).

5-o-*Hydroxyphenyl*-3-*methyl*-1-*phenylpyrazole* (VIII; R = R′ = H).—2-Methyl-4-thionchromone (200 mg.), phenylhydrazine (0·24 c.c.), 2N-sodium hydroxide (4 drops), and ethanol (10 c.c.) were heated on a steam-bath for 2 hours and cooled, and concentrated hydrochloric acid (2 drops) added. The solid (245 mg., 86%) obtained by addition of water was collected and crystallised from dilute alcohol, giving 5-*o*-hydroxyphenyl-3-methyl-1-phenylpyrazole, m. p. 190—191°. This m. p. was not depressed on admixture with a specimen, m. p. 190—191°, prepared from 2-acetoacetylphenol according to Baker and Butt (*loc. cit.*).

5-o-*Hydroxyphenyl*-3 : 4-*dimethyl*-1-*phenylpyrazole* (VIII; R = Me; R′ = H).—2 : 3-Dimethyl-4-thionchromone (1·5 g.), phenylhydrazine (1·7 c.c.), 2N-sodium hydroxide (15 c.c.), and ethanol (30 c.c.) were heated on a steam-bath for 1 hour. After distillation of the ethanol, water was added to the pale yellow solution, which was then neutralised, and the solid product was crystallised from aqueous methanol, giving 5-o-*hydroxyphenyl*-3 : 4-*dimethyl*-1-*phenylpyrazole* (1·15 g., 55%) as colourless prisms, m. p. 210—211° (Found : C, 77·7; H, 6·1; N, 10·6. $C_{17}H_{16}ON_2$ requires, C, 77·3; H, 6·1; N, 10·6%). Simonis and Rosenberg described their product as weakly yellow prisms, m. p. 209°. This pyrazole is soluble in 2N-sodium hydroxide, but does not give a ferric chloride reaction.

Acetylation with acetic anhydride–pyridine gave 5-o-*acetoxyphenyl*-3 : 4-*dimethyl*-1-*phenylpyrazole* (86% yield) as rectangular prisms, m. p. 96—97·5°, from light petroleum (b. p. 60—80°) (Found : C, 75·3; H, 5·9; N, 9·2. $C_{19}H_{18}O_2N_2$ requires C, 74·5; H, 5·9; N, 9·2%).

3(5)-o-*Hydroxyphenyl*-5(3)-*methylpyrazole* (X; R = Me).—(*a*) 2-Methyl-4-thionchromone (250 mg.), ethanol (5 c.c.), and hydrazine hydrate (0·5 c.c.) were shaken at room temperature for 10 minutes, water was added, and the precipitate (223 mg., 90%) crystallised from dilute ethanol. The pyrazole formed needles, m. p. 132—134°, not depressed on admixture with material prepared by method (*b*).

(*b*) *o*-Acetoacetylphenol (245 mg.), hydrazine hydrate (1 c.c.), and ethanol (5 c.c.) were warmed on a steam-bath for 10 minutes, water was added, and the solid (198 mg., 82%) collected and crystallised from aqueous ethanol. The pyrazole formed colourless needles, m. p. 132—134° (Koenigs and Freund, *loc. cit.*, give m. p. 136°). The picrate, yellow needles from ethanol, had m. p. 190° (Koenigs and Freund give m. p. 160°) (Found : C, 47·9; H, 3·1; N, 17·7. Calc. for $C_{10}H_{10}ON_2,C_6H_3O_7N_3$: C, 47·7; H, 3·2; N, 17·4%).

3(5)-o-*Hydroxyphenyl*-4 : 5(3 : 4)-*dimethylpyrazole*.—2 : 3-Dimethyl-4-thionchromone (0·5 g.), hydrazine hydrate (0·8 c.c.), and ethanol (15 c.c.) were heated on a steam-bath for 0·5 hour.

After removal of the ethanol, water was added, and the solid (320 mg.) was crystallised from aqueous ethanol, giving the *pyrazole* as colourless prisms, m. p. 116—118° (Found: C, 70·0; H, 6·4; N, 15·4. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%). It gave an intense purple-green colour with ferric chloride and was soluble in 2N-sodium hydroxide

THE UNIVERSITY, BRISTOL. [*Received, November 30th*, 1951.]

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236. *Synthetic Neuromuscular Blocking Agents. Part III.* Miscellaneous Quaternary Ammonium Salts.*

By E. P. TAYLOR.

Two series of heterocyclic polymethylene- and 5-oxanonamethylene-bis-(quaternary ammonium salts) have been prepared, none of the members of which possesses greater neuromuscular blocking activity in the rabbit than does the corresponding decamethylene derivative. Some compounds related to succinoylcholine (the dicholine ester of succinic acid) and a sulphur analogue of decamethonium iodide have been prepared, but none is as active as the corresponding parent substance.

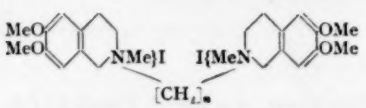
IT was shown (Part I, *J.*, 1951, 1150) that certain heterocyclic decamethylenebis(quaternary ammonium salts) possess strong neuromuscular blocking activity. In Part II * a further series of bis(quaternary ammonium salts) derived from the alkaloid laudanosine was described in which the two quaternary groups were separated by polymethylene and oxapolymethylene chains of various lengths. In this series, the maximum neuromuscular blocking activity in rabbits was found to be associated with a nonamethylene or decamethylene chain, the former being slightly the more active. It was therefore decided to prepare some polymethylene and oxapolymethylene analogues of the two most active compounds described in Part I to ascertain whether the optimal chain length for neuromuscular blocking activity in these two series was the same as in the laudanosinium salts. These compounds (I—IX) were prepared by the two general methods described in Part I. The pharmacological properties were determined by Dr. H. O. J. Collier, and will be described in full elsewhere. In those salts derived from 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxy-2-methyl*iso*quinoline (I—V), the optimal chain length for neuromuscular blocking activity in rabbits appeared to be 10—11, the decamethylene derivative being slightly the more active. The maximum neuromuscular blocking activity in the 1 : 2 : 3 : 4-tetrahydro-6 : 7 : 8-trimethoxy-2-methyl*iso*quinolinium series (VI—IX) was associated with the decamethylene chain. In both of these series, as in the laudanosinium series, introduction of oxygen into the polymethylene chain lowered the pharmacological activity, (V and IX) being considerably less active than (II) and (VI).

At one stage, it appeared possible that bisquaternary salts derived from hydrocotarnine might be of pharmacological interest. For various reasons, however, these compounds were abandoned, and therefore only the octamethylene (X) and nonamethylene (XI) derivatives are described in this paper.

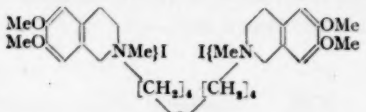
Considerable interest has recently been shown in the neuromuscular blocking activity of certain bischoline esters, in particular succinoylcholine [the dimethiodide of bis-2-dimethylaminoethyl succinate] (XII) and related compounds (see Bovet and his collaborators, *Rend. Ist. Sup. Sanità*, 1949, **12**, Parts I—III; Phillips, *J. Amer. Chem. Soc.*, 1949, **71**, 3264; Walker, *J.*, 1950, 193; Vanderhaeghe, *Nature*, 1951, **167**, 527). It appeared possible therefore that quaternary salts derived from heterocyclic esters of succinic acid might be worth investigation, and accordingly di-8-hydroxyquinolyl succinate dimethosulphate (XIII) was prepared. In this, as in the choline ester, the two quaternary groups are separated by a chain of 10 atoms. This compound, however, had no paralysing activity in rabbits in doses up to 4 mg./kg. (the M.E.D. of the choline ester in rabbits is of the order of 0·15 mg./kg.). It was originally intended to prepare the corresponding 1 : 2 : 3 : 4-tetrahydroquinolyl derivative, since it has been shown in Part I that reduction

* Part II, *J.*, 1952, 142.

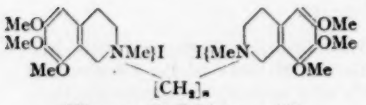
of the heterocyclic nucleus considerably increased the neuromuscular blocking activity. However, in an attempt to prepare the succinate of 1 : 2 : 3 : 4-tetrahydro-8-hydroxy-1-methylquinoline, the bulk of the original base was recovered, and in view of the apparent



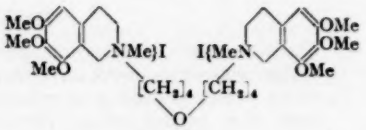
(I; $n = 8$) (III; $n = 11$)
(II; $n = 9$) (IV; $n = 12$)



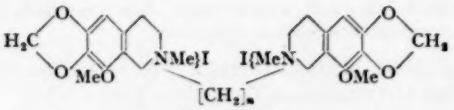
(V)



(VI; $n = 9$) (VII; $n = 11$)
(VIII; $n = 12$)

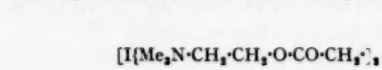


(IX)

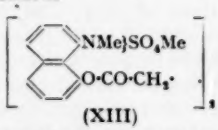


(X; $n = 8$)
(XI; $n = 9$)

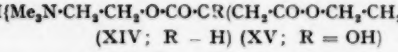
lack of activity of (XIII), this route was abandoned. Dr. Collier suggested examination of quaternary salts derived from 2-dimethylaminoethyl esters of citric and tricarballylic acids, since these possess three quaternary groups separated by chains of 10 atoms. Accordingly, tris-2-dimethylaminoethyl tricarballylate was prepared from tricarballyloyl chloride and 2-dimethylaminoethanol, and converted into the trimethiodide (XIV). However, in mice, this compound possessed only approximately 1/70th of the paralysing activity of the choline ester. The method of preparing (XIV) could not be used for the citric acid derivative (XV) since the chloride of citric acid is unobtainable. Attempts to convert either 2-chloroethyl citrate or the corresponding 2-bromoethyl ester into tris-2-dimethylaminoethyl citrate by treatment with dimethylamine were unsuccessful. Further, an attempt to transesterify ethyl citrate with dimethylaminoethanol failed.



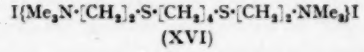
(XII)



(XIII)



(XIV; R = H) (XV; R = OH)



(XVI)

Finally, the effect of replacing methylene groups in decamethonium iodide $I\{Me_3N\cdot[CH_2]_{10}\cdot NMe_3\}I$ by sulphur atoms was investigated. Butane-1 : 4-dithiol, on treatment with 2-dimethylaminoethyl chloride hydrochloride and sodium, gave 1 : 4-bis-2′-dimethylaminoethylthiobutane. The derived dimethiodide (XVI) had approximately 75% of the paralysing activity of decamethonium iodide in mice.

Experimental

(M. p.s and b. p.s are uncorrected. Microanalyses are by Drs. Weiler and Strauss, Oxford. The microanalyses of all quaternary salts were carried out on material dried *in vacuo* at 100°.)

Heterocyclic Bis(quaternary Ammonium Salts).—The following intermediates are new :

1 : 2 : 3 : 4-*Tetrahydro*-6 : 7 : 8-*trimethoxy*isoquinoline, rhombs, m. p. 60—61°, from benzene–light petroleum (b. p. 40—60°), had b. p. 144—145°/0·1 mm. (Found : C, 64·8; H, 7·25; N, 6·1. $C_{13}H_{17}O_3N$ requires C, 64·6; H, 7·7; N, 6·3%). The hydrochloride (Spath, *Monatsh.*, 1921, **42**, 112) became brown at 230° and melted at 242—243° as recorded.

1 : 11-*Bis*-(1 : 2 : 3 : 4-*tetrahydro*-6 : 7 : 8-*trimethoxy*isoquinolino)*undecane dihydrochloride* (from alcohol–ether), m. p. 170—172° (Found: N, 4·4; Cl, 10·3. $C_{35}H_{56}O_6N_2Cl_2$ requires N, 4·2; Cl, 10·6%).

1 : 11-*Bis*-(1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*dimethoxy*isoquinolino)*undecane* (from aqueous alcohol), m. p. 89—91° (Found: C, 73·4; H, 9·4; N, 5·2. $C_{33}H_{50}O_4N_2$ requires C, 73·6; H, 9·4; N, 5·2%).

The following bisquaternary salts were prepared by the general methods previously described (*J.*, 1951, 1151):

Octamethylenebis-(1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*dimethoxy*-2-*methyl*isoquinolinium *iodide*) (I), from methanol–ethanol, microcrystalline, m. p. 225—226° (Found: C, 48·8; H, 6·45; N, 3·4; I, 32·35. $C_{32}H_{50}O_4N_2I_2$ requires C, 49·2; H, 6·5; N, 3·6; I, 32·6%); and the following analogues: *nonamethylene* (II), m. p. 190—192°, from alcohol (Found: C, 49·45; H, 6·3; N, 3·4; I, 31·8. $C_{33}H_{52}O_4N_2I_2$ requires C, 49·9; H, 6·6; N, 3·5; I, 32·0%); *undecamethylene* (III), nodules, m. p. 188—189°, from alcohol (Found: C, 51·15; H, 6·7; N, 3·4; I, 30·4. $C_{35}H_{56}O_4N_2I_2$ requires C, 51·1; H, 6·9; N, 3·4; I, 30·9%); *dodecamethylene* (IV), nodules (from alcohol), containing 3·8% of solvent of crystallisation, which sintered at 55—60° and slowly melted, becoming homogeneous at 173—175° (Found: C, 51·7; H, 7·3; N, 3·3; I, 30·1. $C_{36}H_{58}O_4N_2I_2$ requires C, 51·7; H, 7·0; N, 3·35; I, 30·4%). 5-*Oxanonamethylene* (V), from alcohol, granules, m. p. 201—203° (Found: C, 47·7; H, 6·3; N, 3·6; I, 31·4. $C_{32}H_{50}O_5N_2I_2$ requires C, 48·2; H, 6·3; N, 3·5; I, 31·9%)

Nonamethylenebis-(1 : 2 : 3 : 4-*tetrahydro*-6 : 7 : 8-*trimethoxy*-2-*methyl*isoquinolinium *iodide*) (VI) (from alcohol–ether), m. p. 159—161° (Found: C, 48·8; H, 6·4; N, 3·15; I, 29·9. $C_{35}H_{54}O_6N_2I_2$ requires C, 49·2; H, 6·6; N, 3·3; I, 29·7%); and the following analogues: *undecamethylene* (VII), nodules, m. p. 117—119°, from alcohol–ether (Found: C, 49·9; H, 7·1; N, 3·2; I, 28·3. $C_{37}H_{60}O_6N_2I_2$ requires C, 50·3; H, 6·9; N, 3·2; I, 28·8%); *dodecamethylene* (VIII), granules, m. p. 130—132°, from alcohol–ether (Found: C, 50·6; H, 7·1; N, 2·9; I, 28·1. $C_{38}H_{62}O_6N_2I_2$ requires C, 50·9; H, 7·0; N, 3·1; I, 28·35%). 5-*Oxanonamethylene* (IX), from alcohol, granules, m. p. 191—193° after slight preliminary shrinking (Found: C, 47·5; H, 6·2; N, 3·2; I, 29·4. $C_{34}H_{54}O_7N_2I_2$ requires C, 47·7; H, 6·4; N, 3·3; I, 29·7%).

Octamethylenebis-(1 :2 : 3 : 4-*tetrahydro*-8-*methoxy*-2-*methyl*-6 : 7-*methylenedioxy*isoquinolinium *iodide*) (X), from methyl alcohol, small needles, m. p. 244—246° (decomp.) (Found: C, 47·1; H, 5·6; N, 3·3; I, 31·0. $C_{32}H_{46}O_6N_2I_2$ requires C, 47·5; H, 5·7; N, 3·5; I, 31·4%); and the *nonamethylene* analogue (XI), from methanol–ethanol, m. p. 230—232° (decomp.) (Found: C, 47·9; H, 5·6; N, 3·4; I, 30·7. $C_{33}H_{48}O_6N_2I_2$ requires C, 48·2; H, 5·9; N, 3·4; I, 30·9%).

Substances related to Succinoylcholine.—8-*Hydroxyquinolyl succinate.* Succinoyl chloride (15·5 g., 1 mol.) in dry benzene (50 ml.) was added drop by drop during 20 minutes to a stirred solution of 8-hydroxyquinoline (58 g., 4 mols.) in dry benzene (200 ml.). The mixture became warm, but did not require cooling. After refluxing for 2 hours on the steam-bath and being then left over-night, the mixture was heated and filtered hot, and the residue washed with hot benzene and dried (this residue, dissolved in water and made alkaline with sodium carbonate, gave 28 g. of crude 8-hydroxyquinoline, m. p. 70°). The combined benzene filtrate and washings were evaporated to dryness, giving a white residue (31 g.), m. p. 138—140°, which after recrystallisation from benzene yielded *di*-8-*hydroxyquinolyl succinate* as hard prisms (26 g.), m. p. 141° (Found: C, 70·4; H, 4·4; N, 7·75. $C_{22}H_{16}O_4N_2$ requires C, 71·0; H, 4·3; N, 7·5%). This ester reacted exceedingly slowly with methyl iodide in acetone, benzene, or alcohol. On being heated under reflux in benzene with a 50% excess of methyl sulphate for 24 hours, it gave the *dimethosulphate* (XIII) as colourless needles, m. p. 199—201° (decomp.) (Found: N, 4·45; S, 10·3. $C_{26}H_{28}O_{12}N_2S_2$ requires N, 4·5; S, 10·3%).

Tris-2-*dimethylaminoethyl tricarballylate.* Tricarballyloyl chloride (Emery, *Ber.*, 1889, **22**, 2920) (3·4 g., 1 mol.) in dry ether (15 ml.) was added drop by drop with cooling and shaking to 2-dimethylaminoethanol (4·8 g., *ca.* 3·7 mols.). After 2 hours' gentle refluxing the mixture was set aside overnight; water (20 ml.) was then added, and the mixture thoroughly shaken. The aqueous layer was then separated, treated with an equal volume of saturated potassium carbonate solution, and extracted three times with ether, and the extract dried (Na_2SO_4). The ether was then removed and the residue distilled *in vacuo*, giving the *ester* (2·5 g.), b. p. 178—180°/0·5 mm. (Found: C, 55·8; H, 8·7; N, 10·0. $C_{18}H_{35}O_6N_3$ requires C, 55·5; H, 9·1; N, 10·8%). The *trimethiodide* (XIV) separated from methanol–ethanol as a microcrystalline powder, m. p. 207° (decomp.) (Found: C, 30·95; H, 5·45; N, 5·25; I, 46·2. $C_{21}H_{44}O_6N_3I_3$ requires C, 30·9; H, 5·4; N, 5·15; I, 46·75%).

1 : 2 : 3 : 4-Tetrahydro-8-hydroxy-1-methylquinoline (Fischer, *Ber.*, 1883, **16**, 714) gave a

methiodide, large sheaves of flat needles (from alcohol), m. p. 220—221° (decomp.) (Found: C, 43·3; H, 5·4; N, 4·6; I, 41·5. Calc. for $C_{11}H_{16}ONI$: C, 43·3; H, 5·3; N, 4·6; I, 41·6%). Fischer and Kohn (*ibid.*, 1886, **19**, 1041) describe it as prisms, m. p. 215—216°.

1 : 4-*Bis*-2'-*dimethylaminoethylthiobutane*.—Butane-1 : 4-dithiol (von Braun, *Ber.*, 1909, **42**, 4572) (9 g., 1 mol.) and 2-dimethylaminoethyl chloride hydrochloride (27 g., *ca.* 2·5 mol.) were dissolved in methanol (200 ml.), and the solution was treated at −10° with a solution of sodium (7·64 g., 4·5 mols.) in methyl alcohol (130 ml.). The reaction mixture was then worked up as described by Clinton, Salvador, Laskowski, and Suter [*J. Amer. Chem. Soc.*, 1948, **70**, 951; method A for the preparation of 2-(2-diethylaminoethylthio)ethylamine]. The *dithio*-derivative (5 g.), b. p. 124—126°/0·2 mm., was obtained (Found: C, 54·3; H, 10·7; N, 10·35; S, 24·1. $C_{12}H_{26}N_2S_2$ requires C, 54·55; H, 10·7; N, 10·6; S, 24·2%).

The *dimethiodide* (XVI) crystallised from methanol–ethanol as needles, m. p. 221° (decomp.) (Found: C, 30·9; H, 6·3; N, 5·2; S, 11·3; I, 46·3. $C_{14}H_{34}N_2S_2I_2$ requires C, 30·7; H, 6·25; N, 5·1; S, 11·7; I, 46·35%)

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237. *The Electrolytic Dissociation of Strontium Iodate and of Strontium Hydroxide.*

By C. A. Colman-Porter and C. B. Monk.

The conductivities of dilute aqueous solutions of strontium iodate at 25° have been measured. From the results, a value of $K = 0·10$ is obtained for the dissociation constant of the intermediate ion $Sr(IO_3)^+$. The solubility of the salt in water and in sodium hydroxide solutions at 25° has also been measured and used to derive the dissociation constant of $Sr(OH)^+$. The average value of 0·11 agrees closely with that calculated from an equation given by Davies for the strong hydroxides which assumes that interaction occurs with the unhydrated cations.

The sparingly soluble iodates of calcium and barium have been used by Davies (*e.g.*, *J.*, 1951, 233; *Trans. Faraday Soc.*, 1949, **45**, 770) for quantitative studies of ion association between these cations and various anions. Some general trends have been noticed in the results obtained; for instance, the dissociation constants of their hydroxides (as well as those of other cations which form "strong" hydroxides) are related to the crystallographic radii of the cations (Davies, *J.*, 1951, 1256). Similar trends are found with organic anions such as malonate (Stock and Davies, *J.*, 1949, 1371), but with simple inorganic anions such as the iodates and nitrates, the trends are in the reverse direction, namely, in the order of size of the hydrated cations. These factors, together with the effect of increasing valency forces, have been discussed previously (Jones, Monk, and Davies, *J.*, 1949, 2693). The intermediate size of the strontium ion, in both its hydrated and its unhydrated form, between calcium and barium should prove of some value in providing further information on the nature of these factors which influence ion-pair formation.

In order to obtain dissociation constants of strontium salts by the solubility method, we have prepared strontium iodate crystals in a suitable form, and have obtained the second dissociation constant of this from some conductivity measurements on its aqueous solutions. The solubility in sodium hydroxide solutions has also been used to derive the second dissociation constant of strontium hydroxide.

Experimental

Suitably sized crystals of strontium iodate were formed by allowing approximately 0·1N-solutions of "AnalaR" strontium chloride and of "AnalaR" potassium iodate to drip very slowly into 1 l. of distilled water at room temperature. Heating a sample of the crystals (dried

by washing with acetone) to 150° showed these to be the monohydrate $Sr(IO_3)_2,H_2O$. Crystals prepared by allowing the parent solutions to drip into water kept at 80° proved to be unsatisfactory; they had a lower solubility which showed considerable variation, and tended to break up.

The solubility of the hydrated crystals in water at 25° was measured by packing the crystals in the type of saturator described by Money and Davies (*J.*, 1934, 401) and titrating 20-ml. samples of the saturated solution against 0·06N-sodium thiosulphate that had been standardised with potassium iodate. The solubility of the salt in sodium hydroxide solutions was determined similarly. For the latter solutions a stock solution of " AnalaR " carbonate-free alkali was standardised with potassium hydrogen phthalate. Before samples were taken for titration, three separate portions were allowed to percolate through the iodate column, and the pipette was washed and dried to remove any carbonate formed.

The conductivity measurements were made with the apparatus described previously (Davies and Monk, *J.*, 1949, 413). Conductivity water was passed through the saturator; the first washings were rejected and a quantity was collected in a flask containing sufficient water to ensure that crystals would not separate out at room temperature. The concentration of this stock solution was found by titration against sodium thiosulphate standardised with potassium iodate, both the strontium and the potassium solutions being weighed. Two separate stock solutions were made.

The conductivity data are reported in Table 1, where C is the concentration in g.-equiv. per l., and Λ is the equivalent conductivity. The solubility measurements and resultant calculations are given in Table 2.

TABLE 1. *The conductivity of strontium iodate solutions at* 25°.

10^4C	Λ	$10^3\alpha$	K	10^4C	Λ	$10^3\alpha$	K
2·3419	97·57	2·37	0·09$_0$	7·3866	95·38	6·63	0·09$_5$
5·2187	96·28	3·85	0·11	9·4788	94·76	7·33	0·11
7·3603	94·52	6·15	0·10				

TABLE 2. *The solubility of strontium iodate in sodium hydroxide solutions* (concns. in m.-mols. or mg.-ions per l.).

Soly.	NaOH	$[Sr(IO_3)^+]$	$[NaIO_3]$	$[Sr(OH)^+]$	10^3I	K
5·87	—	0·37	—	—	16·87	—
6·55	16·70	0·37	0·05	0·41	34·74	0·115
6·73	22·31	0·36	0·07	0·53	40·65	0·115
6·98	30·21	0·36	0·09	0·74	48·86	0·106
7·40	45·99	0·35	0·14	1·06	65·23	0·106

DISCUSSION

The Onsager limiting conductivity equation for strontium iodate in water at 25° is $\Lambda = 100{\cdot}21 - 132{\cdot}83\ I^{\frac{1}{2}}$, where Λ is the equivalent conductivity, and I the ionic strength. The equivalent conductivity of 100·21 at zero concentration is derived from 59·46 for the strontium ion (Shedlovsky and Brown, *J. Amer. Chem. Soc.*, 1934, **56**, 1066) and 40·75 for the iodate ion (Monk, *ibid.*, 1948, **70**, 3281). Comparison with the experimental conductivities shows that the theoretical values are slightly higher, and this may be attributed to the presence of the ion-pair $Sr(IO_3)^+$. The dissociation constant of this ion may be calculated by the method of Righellato and Davies (*Trans. Faraday Soc.*, 1930, **26**, 592) for 2 : 1-valent types of electrolytes. The exact mobility of the ion-pair is not known, but comparison of similar types of ions of valencies 1 and 2 suggests that it has a value of 0·5—0·65 of that of the strontium ion. We have assumed that the $Sr(IO_3)^+$ ion has the lower value, *i.e.*, its conductivity at zero concentration is equal to half that of the strontium ion, so that the corresponding Onsager equation for the dissociation process $Sr(IO_3)^+ \rightleftharpoons Sr^{2+} + IO_3^-$ is $\Lambda = 70{\cdot}48 - 76{\cdot}38\ I^{\frac{1}{2}}$, and if in any particular solution we assume that α is the fraction of strontium ions which associate to form $Sr(IO_3)^+$ ions, combination of the two equations gives an expression from which α may be calculated, namely,

$$\Lambda\ (\text{obs.}) = 100{\cdot}21 - 132{\cdot}83\ I^{\frac{1}{2}} - \alpha(64{\cdot}97 - 94{\cdot}64\ I^{\frac{1}{2}})$$

The ionic strength is given by $I = C(1{\cdot}5 - \alpha)$. The values of α thereby obtained are given in Table 1 together with the dissociation constants for the equilibrium

$K = [Sr^{2+}][IO_3^-]f_1f_2/[Sr(IO_3)^+]f_3$, the limiting Debye–Hückel activity coefficient expression $-\log f_i = 0{\cdot}509z_i^2I^{\frac{1}{2}}$ being used (where z_i is the ion valency). The average of $K = 0{\cdot}10$ lies between those of 0·13 for calcium (Wise and Davies, *J.*, 1938, 273) and 0·08 for barium (MacDougall and Davies, *J.*, 1935, 1416). In all three cases the results are dependent to some extent on the assumption previously referred to concerning intermediate ion mobilities, and the absence of significant drifts in the K data over a range of concentrations probably supports the assumption. In any case, since all three constants have been calculated on the same basis, the results are at least qualitatively comparable. Broadly speaking, the general order of these constants is in the same direction as the radii of the hydrated cations if one takes the cation mobilities as a criterion. The comparison is only approximate, however, since the calcium and strontium mobilities are almost identical.

The batch of strontium iodate crystals used for the solubility measurements reported in Table 2 had a solubility of 5·87 m.-mol. per l. in water at 25°. This remained constant, although a second batch prepared in a similar fashion showed a solubility of 5·89. Account being taken of the presence of $Sr(IO_3)^+$ ions, the activity solubility product (*i.e.*, of the first batch) is $3{\cdot}289 \times 10^{-7}$. In calculating this, use has been made of the activity coefficient expression used by Davies for similar work (*J.*, 1938, 2093), namely, $-\log f_i = 0{\cdot}5z_i^2\{I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - 0{\cdot}2I\}$. On this basis, and with allowance for the slight association that occurs between sodium and iodate ions, for which $K = 3{\cdot}0$ (MacDougall and Davies, *loc. cit.*), the concentrations of $Sr(OH)^+$ ion pairs were calculated by successive approximations. From these, the dissociation constant of the equilibrium $Sr(OH)^+ = Sr^{2+} + OH^-$ has been derived. These results are shown in the last column of Table 2, and the average is 0·11.

Davies, in a discussion of the dissociation of the metal hydroxides (*J.*, 1951, 1256), has shown that the dissociation constants of those which are "strong" can be expressed by $pK = 0{\cdot}607z^2/r - 1{\cdot}150$, where r is the crystallographic radius of the cation in Å, and z is its valency. Pauling ("Nature of the Chemical Bond," 2nd edn., Cornell Univ. Press, p. 346) gives r as 1·13 Å for strontium, so Davies's relation predicts a K of 0·10, in good agreement with the experimental value. Accordingly, the dissociation constant of strontium hydroxide is also related to the size of the unhydrated cation.

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238. *The Condensed Phosphoric Acids and Their Salts. Part VI.* Dissociation Constants of Strontium Trimetaphosphate and Tetrametaphosphate.*

By C. B. MONK.

The conductivities of strontium chloride solutions containing sodium trimetaphosphate or sodium tetrametaphosphate have been used to calculate the dissociation constants of the ion-pairs $SrP_3O_9^-$ and $SrP_4O_{12}^{2-}$. The results are supported by the solubilities of strontium iodate in solutions of these sodium salts, and are compared with those of the other alkaline-earth metals in terms of ion radii.

IN Parts IV and V of this series (Jones, Monk, and Davies, *J.*, 1949, 2693; Jones and Monk, *loc. cit.**) the dissociation constants of the ion-pairs formed between some M^{2+} ions and the trimetaphosphate ($P_3O_9^{3-}$) and tetrametaphosphate ($P_4O_{12}^{4-}$) ions were reported. The method used consisted of mixing dilute solutions of the chlorides MCl_2 with solutions of the sodium metaphosphates, and calculating the extent of ion-association from the difference between the calculated and observed specific conductivities. The solubility of calcium iodate in solutions of the sodium metaphosphates gave confirmatory evidence in the case of calcium.

* Part V, *J.*, 1950, 3475.

It was remarked that the results of magnesium, calcium, and barium were somewhat irregular when compared with the nitrates, iodates, and hydroxides of these cations. With the first two of these anions, the dissociation constants are related to the sizes of the hydrated cations, *i.e.*, Mg>Ca>Ba, whereas those of the hydroxides follow the reverse order, namely, according to the radii of the unhydrated cations. This latter aspect has been examined in detail by Davies (*J.*, 1951, 1256), and the value given for strontium hydroxide in the preceding paper fits in with this view. In Parts IV and V (*locc. cit.*) it was suggested that the stronger electrostatic forces resulting from the higher valencies of the metaphosphate ions can at least partly counterbalance the solvation forces of the cations and account for the dissociation constants following an order between the two types discussed above. Accordingly, the intermediate position of strontium between calcium and barium should help to clarify this point.

The dissociation constants of the ion-pairs $SrP_3O_9^-$ and $SrP_4O_{12}^{2-}$ were obtained by the methods used previously (Parts IV and V, *locc. cit.*), namely, from the conductivities of mixed solutions of strontium chloride and the sodium metaphosphates. In addition, supporting evidence has been obtained from the solubility of strontium iodate in solutions of these sodium salts.

Experimental

"AnalaR" strontium chloride was used in the conductivity measurements, which were made with the equipment described previously (Davies, *J.*, 1937, 432; Davies and Monk, *J.*, 1949, 413). Sodium trimetaphosphate was prepared by the method described in Part I (Davies and Monk, *loc. cit.*), and the sodium tetrametaphosphate was taken from the sample described in Part V (*loc. cit.*). The solubility measurements were made as detailed in the preceding paper. A trace of acetic acid was added to the solvent solutions to overcome drifts in the solubilities due to slight hydrolysis.

Discussion

The conductivity data, which are reported in Tables 1 and 2, have been interpreted by the previously described processes (Parts IV and V, *locc. cit.*), the same nomenclature being used. In the tables, c_1 is the concentration of sodium metaphosphate in equiv. per l., c_2 is that of strontium chloride, a and a_1 are those of the $NaP_3O_9^{2-}$ and $NaP_4O_{12}^{3-}$ ion-pairs, b is that of $SrP_3O_9^-$ and $SrP_4O_{12}^{2-}$, d represents $Sr_2P_4O_{12}$, and e represents $NaSrP_4O_{12}^-$. The same dissociation constants were used as before in calculating the concentrations of these ion-pairs, except, of course, those being obtained, namely, $SrP_3O_9^-$ and $SrP_4O_{12}^{2-}$. The derived constants, K, of the latter are given in the last columns of the tables. As before, I represents the ionic strength, and κ the specific conductivity. The limiting mobility of the strontium ion was taken as 59·46 (Shedlovsky and Brown, *J. Amer. Chem. Soc.*, 1934, **56**, 1066).

Table 1. *Conductivities of* $Na_3P_3O_9$ *solutions containing* $SrCl_2$.

10^4c_1	10^4c_2	10^6a	10^4b	$10^4\kappa$ (calc.)	$10^4\kappa$ (obs.)	10^3I	10^4K
8·509	3·853	2·2	0·426	1·5569	1·4215	2·02	4·42
8·418	7·343	1·9	0·683	1·9845	1·7695	2·37	4·64
11·428	8·967	3·1	1·109	2·5418	2·2243	3·01	4·33
11·355	12·583	2·8	1·265	2·9809	2·5893	3·39	4·36

Table 2. *Conductivities of* $Na_4P_4O_{12}$ *solutions containing* $SrCl_2$.

10^4c_1	10^4c_2	10^5a_1	10^6a	10^4b	10^6d	10^7e	$10^4\kappa$ (calc.)	$10^4\kappa$ (obs.)	10^3I	10^4K
6·856	1·600	0·86	5·1	0·696	—	2·0	1·1141	0·8619	1·50	7·0
6·825	3·071	0·88	2·7	1·177	1·5	3·4	1·3080	0·8788	1·21	7 0
13·550	11·062	3·16	2·1	3·092	21·4	17·0	3·1617	2·0431	2·45	7·0

The solubility results reported in Tables 3 and 4 have also been obtained by previously established methods (Parts I and V, *locc. cit.*). In these tables, the concentrations are all multiplied by 10^3. Trial and error methods indicated that a reasonable value for the dissociation constant of $Sr_2P_4O_{12}$ is about 0·0035 and this was used in calculating the amounts of this which are listed in Table 4. When using 0·002, the value adopted in the case of calcium (Part I, *loc, cit.*), marked drifts were found in the evaluation of K for $SrP_4O_{12}^{2-}$.

TABLE 3. *Solubility of* $Sr(IO_3)_2$ *in* $Na_3P_3O_9$ *solutions.*

(Concentrations × 10^3)

$Na_3P_3O_9$	Soly.	$[Sr(IO_3)^+]$	$[NaP_3O_9^{2-}]$	$[NaIO_3]$	$[SrP_3O_9^-]$	10^3I	10^4K
—	5·87	0·37	—	—	—	16·87	—
5·46	7·54	0·35	0·20	0·05	2·80	37·29	4·59
6·75	7·88	0·31	0·30	0·07	3·28	42·87	4·36
8·24	8·20	0·31	0·44	0·09	3·64	50·17	4·45
10·61	8·67	0·30	0·71	0·11	4·21	61·57	4·28

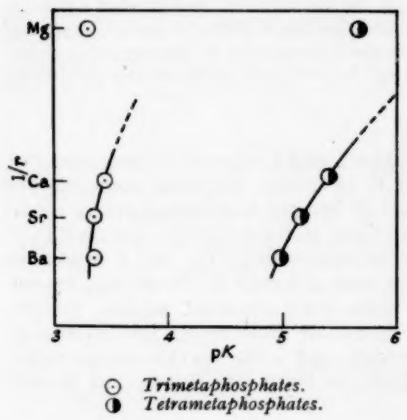
TABLE 4. *Solubility of* $Sr(IO_3)_2$ *in* $Na_4P_4O_{12}$ *solutions.*

(Concentrations × 10^3)

$Na_4P_4O_{12}$	Soly.	$[Sr(IO_3)^+]$	$[NaP_4O_{12}^{3-}]$	$[NaIO_3]$	$[SrP_4O_{12}^{2-}]$	$[Sr_2P_4O_{12}]$	$[NaSrP_4O_{12}^-]$	10^3I	10^6K
5·71	9·33	0·26	0·12	0·09	4·30	0·84	0·24	37·14	8·1
8·50	10·87	0·23	0·48	0·16	6·09	0·84	0·45	51·77	10·2
11·87	12·91	0·20	0·87	0·24	8·42	0·78	0·78	68·78	6·6

The average K for $SrP_3O_9^-$ is $4{\cdot}44 \times 10^{-4}$ from conductivities and $4{\cdot}42 \times 10^{-4}$ from solubilities. The average K for $SrP_4O_{12}^{2-}$ is $7{\cdot}0 \times 10^{-6}$ from conductivities and $8{\cdot}3 \times 10^{-6}$ (approx.) from solubilities; the former of these is probably the more correct since the solubility method involves more assumptions, and these influence the results considerably.

For the purposes of comparison, these results, together with those which have been obtained with the other alkaline-earth metals (Parts IV and V, *locc. cit.*), are given in Table 5. The strontium results lie between those for calcium and barium, and the order with these three follows the same trend as the crystallographic radii of the cations, r, which are also placed in the table (these are taken from Pauling's "Nature of the Chemical Bond," 2nd edn., Cornell Univ. Press, p. 346). With both the phosphates, the magnesium figures show departure from this rule. The differing results for magnesium may be perhaps interpreted as follows. Since the Mg^{2+} ion has the lowest limiting mobility of the series—the figures (Shedlovsky and Brown, *loc. cit.*) are given in Table 5—the hydrated Mg^{2+} ion is the largest, whereas it has the smallest crystallographic radius, and is consequently the most heavily hydrated. Apparently the cation–anion interaction has less ability to overcome the hydration with this cation than with the other cations, and this is manifest in the irregular order of the dissociation constants. This irregularity is illustrated by the figure, where $1/r$ (the reciprocal of the crystallographic radius) is plotted against pK. The smooth curves given by calcium, strontium, and barium are similar to those given by the strong hydroxides (Davies, *loc. cit.*, 1951), which suggests that with these the energy of cation–anion interaction energy is sufficient to overcome the energy of cation solvation. In order to fit on to these curves, the pK's of the magnesium salts would have to be about one unit higher.



⊙ *Trimetaphosphates.*
◑ *Tetrametaphosphates.*

To get some idea of the sizes of the ion-pairs, the "Bjerrum distances" of closest approach of the cations and anions are given in Table 5. Subtraction of the crystallographic radii, r, from the Bjerrum distances should give the anion radii if the interaction is between the unhydrated ions. The results for the trimetaphosphates are $3{\cdot}2 \pm 0{\cdot}1$ Å, with the exception of Mg (3·9 Å). From Stokes's law and the limiting mobility of the anion (Part I, *loc. cit.*), which is given in Table 5, the radius of the trimetaphosphate ion is 3·29 Å, in excellent agreement with the above figure of 3·2 Å. It would therefore appear that the trimetaphosphate ion is not hydrated, and that the assumption of interaction with the unhydrated cations in the instances of Ca, Sr, and Ba is supported, while the hydration shell of the magnesium ion is only partly penetrated.

On applying the same tests to the tetrametaphosphates, the differences between the Bjerrum distances and the crystallographic radii are 2·6 Å with Ca, Sr, and Ba, whereas the Mg value is 3·1 Å. Stokes's law, on the other hand, indicates that the tetrametaphosphate ion has a radius of 3·91 Å, so that the good agreement found with the trimetaphosphates is not upheld here. It is possible that, since we have two stages of association in these cases,

TABLE 5.

	Trimetaphosphates		Tetrametaphosphates			Ion radii (Å)	
Ions	10^4K	Bjerrum distances (Å)	10^4K	Bjerrum distances (Å)	Λ_i°	Stokes's law	Cryst.
Magnesium	4·89	$4·5_3$	6·7	$3·7_3$	53·06	3·45	0·65
Calcium	3·56	$4·2_0$	3·9	$3·5_5$	59·50	3·08	0·99
Strontium	4·43	$4·4_2$	7·0	$3·7_4$	59·46	3·08	1·13
Barium	4·50	$4·4_4$	10·3	$3·8_9$	63·64	2·88	1·35
Trimetaphosphate	—	—	—	—	83·59	3·29	—
Tetrametaphosphate	—	—	—	—	93·69	3·91	—

the probability factor in the Bjerrum expression is not valid in such systems. In spite of this disagreement, the view that the radius of the magnesium ion in the ion-pair lies between that of the bare ion and that when it is fully hydrated is qualitatively supported.

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239. *The Condensed Phosphoric Acids and Their Salts. Part VII.* Ion Association between Some Tervalent Cations and the Tri- and Tetra-metaphosphates.*

By C. B. MONK.

The extent of ion-pair formation between lanthanum, some complex cobaltic cations, and the trimetaphosphate and tetrametaphosphate ions has been calculated from the conductivities of mixed solutions of the cation chlorides containing solutions of the sodium metaphosphates. The resulting dissociation constants are qualitatively related to the cation sizes.

IN continuation of previous studies of the extent of ion-pair formation between cations and $P_3O_9^{3-}$ and $P_4O_{12}^{4-}$ ions (see Part VI *), attention has now been directed to the kind of interaction that occurs when tervalent cations are used. The same procedure has been adopted as in the previous cases, namely use of the differences between the calculated and observed specific conductivities of mixtures of the sodium metaphosphates and the cation chlorides.

Considering, first, the trimetaphosphates, where MP_3O_9 ion-pairs are formed (M representing a tervalent cation), for a solution containing c_1 equiv. per l. of sodium trimetaphosphate and c_2 of MCl_3, if a g.-ions of $NaP_3O_9^{2-}$, b g.-ions of MCl^{2+}, and d g.-ions of MP_3O_9 are present per l., then

$$10^3\kappa\,(\text{obs.}) = \Lambda_{Na^+}(c_1 - a) + 3\Lambda_{P_3O_9^{3-}}(c_1/3 - a - d) + 2a\Lambda_{NaP_3O_9^{2-}} + 3\Lambda_{M^{3+}}(c_2/3 - b - d) + \Lambda_{Cl^-} - (c_2 - d) + 2b\Lambda_{MCl^{2+}}$$

where κ is the specific conductivity. The value of a is slightly different from what it would be in sodium trimetaphosphate solutions of the same ionic strength as the mixtures, but for the purposes of calculation this difference may be neglected, and similarly for b (both a and b are relatively small). Accordingly, the above expression becomes

$$10^3\kappa\,(\text{obs.}) = c_1\Lambda_{Na_3P_3O_9} + c_2\Lambda_{MCl_3} - 3d(\Lambda_{P_3O_9^{3-}} + \Lambda_{M^{3+}})$$

where the first two equivalent conductivities (Λ) can be found from known data, and those of the two ions from the appropriate Onsager equation $\Lambda_i = \Lambda_i^\circ - BI^{\frac{1}{2}}$, I being the ionic

* Part VI, preceding paper.

strength and B the theoretical Onsager value. The values of Λ_i°, the equivalent ionic conductivity at zero ionic strength, and of B are listed in Table 2. The ionic strength is given by

$$I = 0{\cdot}5\{4c_1 + 4c_2 - 6a - 5d - 18d\}$$

a being obtained from the known dissociation constant of $NaP_3O_9^{2-}$ (Davies and Monk, *J.*, 1949, 413) and b from the corresponding data for MCl^{2+} in the cases of the complex cobaltic chlorides (Jenkins and Monk, *J.*, 1951, 68). The other tervalent chloride used, lanthanum chloride, appears to ionise fully in the concentration range used here (James and Monk, *Trans. Faraday Soc.*, 1950, **46**, 141). The true values of a, b, and d were found by successive approximations.

If no MP_3O_9 were formed, we would have

$$10^3\,\kappa\ (\text{calc.}) = c_1\Lambda_{Na_3P_3O_9} + c_2\Lambda_{MCl_3}$$

Hence, by subtraction,

$$10^3\{\kappa\ (\text{calc.}) - \kappa\ (\text{obs.})\} = 3b(\Lambda_{P_3O_9^{3-}} + \Lambda_{M^{3+}})$$

which gives b. The final values of a, b, and d thus obtained were used in calculating the dissociation constants of the equilibria

$$MP_3O_9 \rightleftharpoons M^{3+} + P_3O_9^{3-},$$

i.e.,

$$K = (c_2/3 - b - d)(c_1/3 - a - d)f_1f_2/b$$

where the ion activity coefficients f_1 and f_2 are found from the Debye–Hückel limiting equation $-\log f_i = 0{\cdot}509z_i^2I^{\frac{1}{2}}$, z_i being the ion valency. The calculated specific conductivities were obtained from known data (Davies and Monk; Jenkins and Monk; James and Monk, *locc. cit.*) for sodium trimetaphosphate, cobaltammine chlorides, and lanthanum chloride respectively. The average dissociation constants from Table 1 (which contains the experimental results and the calculated data) are given in Table 4.

TABLE 1. *Data for the dissociation constants of* MP_3O_9.

10^4c_1	10^4c_2	10^4a	10^5b	10^5d	$10^4\,\kappa$ (calc.)	$10^4\,\kappa$ (obs.)	10^3I	10^5K
			M = Lanthanum					
17·640	17·465	1·0	53·23	—	4·5645	2·3152	2·22	0·19
9·614	6·303	2·0	20·29	—	2·0851	1·2103	1·35	0·19
17·938	11·483	5·0	37·27	—	3·7965	2·2006	2·51	0·21
17·798	14·292	2·5	45·78	—	4·1492	2·2157	2·29	0·20
			M = Hexamminocobalt(III)					
11·709	6·926	2·9	15·93	1·1	2·5768	1·7668	2·28	3·69
11·498	14·786	1·5	25·41	7·4	3·8403	2·5101	2·95	3·70
10·028	4·113	2·6	9·84	0·4	1·9263	1·4231	1·94	3·58
9·999	6·332	2·1	14·09	1·0	2·2844	1·5646	2·00	3·64
			M = Trisethylenediaminocobalt(III)					
4·062	2·909	0·4	5·01	1·0	0·9334	0·7076	0·94	4·07
4·023	5·159	0·3	7·37	1·2	1·2435	0·9134	1·16	3·90
3·247	1·228	0·3	2·27	0·7	0·5934	0·4904	0·67	3·80
3·229	2·495	0·3	3·97	0·8	0·7718	0·5918	0·78	3·99
			M = Trispropylenediaminocobalt(III)					
9·768	7·360	2·5	6·60	3·6	2·1464	1·8788	2·81	24·4
9·690	15·201	2·0	10·22	15·0	3·0893	2·6837	4·06	21·7
11·705	5·524	3·5	5·58	1·9	2·0269	1·8007	2·73	22·4
10·583	16·918	2·3	11·48	18·0	2·9411	2·3949	4·46	21·7

TABLE 2. *Constants used in the calculations.*

	La^{3+}	$Co(NH_3)_6^{3+}$	$Co(en)_3^{3+}$	$Co(pn)_3^{3+}$	$P_3O_9^{3-}$	$P_4O_{12}^{4-}$
Λ_i°	69·61	99·20	74·71	65·06	83·59	93·69
B	127·6	147·5	130·9	124·7	141·0	190·8
	$LaCl_3$	$Co(NH_3)_6Cl_3$	$Co(en)_3Cl_3$	$Co(pn)_3Cl_3$	$Na_3P_3O_9$	$Na_4P_4O_{12}$
Λ°	145·95	175·55	151·05	141·40	133·70	143·80
E	198·6	260·0	254·0	232·0	212·0	313·0

(E represents the experimental slope in the equation $\Lambda = \Lambda^\circ - EI^{\frac{1}{2}}$; for B, see p. 1317.)

The method of calculating the concentrations of $MP_4O_{12}^-$ ion-pairs in mixtures of MCl_3 and $Na_4P_4O_{12}$ is similar to that described above, except that the type of assumption used previously (Part V, *loc. cit.*) is used, namely, that the equivalent conductivity of the $MP_4O_{12}^-$ ion is one-quarter of that of the $P_4O_{12}^{4-}$ ion. The ionic-strength expression is

$$I = 0{\cdot}5\{5c_1 + 4c_2 - 8a - 9c - 24b\}$$

where c_1 now represents the equivalent concentration of sodium tetrametaphosphate c_2 is that of MCl_3, a and b are the $NaP_4O_{12}^{3-}$ and $MP_4O_{12}^-$ concentrations respectively. The latter is obtained from

$$10^3\{\kappa \text{ (calc.)} - \kappa \text{ (obs.)}\} = b(3{\cdot}75\Lambda_{P_4O_{12}^{4-}} + 3\Lambda_{M^{3+}})$$

The dissociation constants K were calculated from

$$K = (c_2/3 - b - d)(c_1/4 - a - b)f_1f_2/bf_3$$

where the activity coefficients f_i were calculated from the expression given previously. The data are given in Table 3.

TABLE 3. *Data for the dissociation constants of* $MP_4O_{12}^-$.

10^4c_1	10^4c_2	10^4a	10^5b	10^5d	$10^4\kappa$ (calc.)	$10^4\kappa$ (obs.)	10^3I	10^4K
			M = Lanthanum					
11·454	9·155	0·7	27·83	—	2·7815	1·3351	1·35	0·25
9·944	7·075	1·4	22·94	—	2·3073	1·1076	1·14	0·19
			M = Hexamminocobalt(III)					
10·735	11·741	1·0	25·51	3·0	3·3214	1·7962	1·95	1·85
13·387	8·680	6·0	26·55	0·4	3·1699	1·5802	1·87	1·65
13·238	10·334	3·4	29·28	1·0	3·4246	1·6700	1·85	1·80
13·174	11·036	2·8	29·84	1·6	3·5268	1·7410	1·90	1·88
			M = Trisethylediaminocobalt(III)					
10·537	6·682	4·4	20·35	0·4	2·3305	1·2470	1·51	1·72
10·476	9·380	1·5	24·34	2·2	2·6999	1·4056	1·56	1·54
11·490	6·043	8·0	18·90	0·2	2·3484	1·3493	1·78	1·78
11·422	8·822	2·5	25·12	1·0	2·7431	1·4087	1·59	1·73
			M = Trispropylenediaminocobalt(III)					
8·556	5·346	6·5	9·87	1·2	1·8111	1·3196	1·99	24·5
8·508	7·359	5·5	11·93	2·5	2·0576	1·4699	2·15	24·7
9·980	5·745	9·0	11·00	0·5	2·0344	1·4900	2·29	25·0
9·832	11·098	5·5	15·58	6·0	2·6847	1·9229	2·79	25·6

DISCUSSION

A summary of the dissociation constants is given in Table 4, together with those of the corresponding sulphates (Jenkins and Monk, *loc. cit.*). In each series it will be noticed that

TABLE 4.

	La^{3+}	$Co(NH_3)^{3+}$	$Co(en)_3^{3+}$	$Co(pn)_3^{3+}$
	Average dissociation constants			
Sulphates ($\times 10^4$)	2·0	2·77	3·55	17·5
Trimetaphosphates ($\times 10^5$)	0·20	3·65	3·94	22·6
Tetrametaphosphates ($\times 10^6$)	0·22	1·80	1·69	25·6
	Bjerrum distances (Å)			
Sulphates	3·8	4·0	4·2	7·3
Trimetaphosphates	3·9	5·3	5·3	7·7
Tetrametaphosphates	4·7	5·5	5·5	7·6
	Radii of ion-pairs from Stokes's law (Å)			
Sulphates	6·2	5·1	6·0	6·5
Trimetaphosphates	7·2	6·1	7·0	7·5
Tetrametaphosphates	7·9	6·7	7·6	8·1

the values for lanthanum are the smallest, those for $Co(NH_3)_6^{3+}$ and $Co(en)_3^{3+}$ show little difference, and those for $Co(pn)_3^{3+}$ are much the largest. The Bjerrum distances of closest approach of the ions, and the radii of the ion-pairs as calculated by Stokes's law from the limiting mobilities of the ions, are also included in Table 4.

The difference between the radii of the ion-pairs as calculated by the two methods is most marked with the lanthanum series, and supports the suggestion made previously (Part IV, *loc. cit.*; also Part VI), namely, that with these high valency forces the energy of interaction is sufficiently large to overcome, at least, in part, the energy of ion-hydration. The lanthanum ion is undoubtedly heavily hydrated, since the crystallographic radius is 1·15 Å (Pauling, " Nature of the Chemical Bond," Cornell Univ. Press, 2nd edn., p. 346) whereas application of Stokes's law gives the ion radius as 3·95 Å. Using the 1·15 Å value together with the Stokes's law values for the three anions, we get 3·4, 4·4, and 5·1 Å for the radii of the lanthanum ion-pairs, in much better agreement with the Bjerrum distances. This would only be admissible if the anions were hydrated to a relatively small extent, and this conclusion is upheld by the trimetaphosphate results (Part VI, *loc. cit.*). Some reserve must be placed on this conclusion, however, since the comparison with the tetrametaphosphates of bivalent metals does not fit into this scheme (probably because of the complication that two equilibria are involved).

The relatively close agreement between the Bjerrum and the Stokes's law distances found with the complex cobaltic ions indicates that both cations and anions are comparatively unhydrated. This applies particularly to the last of these cations, $Co(pn)_3^{3+}$, where, by analogy with the alkali and alkaline-earth metals, we would expect the largest ion of the series to be the least solvated.

Experimental

The conductivity equipment used was that referred to in Part VI, where the sources of the sodium metaphosphates were also given. The lanthanum chloride was made by boiling an excess of " Spec-pure " lanthanum oxide with a 50% solution of A.R. hydrochloric acid until the pH was about 5·5, filtering it, and diluting it with conductivity water. The complex cobaltic salts were taken from samples used for previous conductivity work (Jenkins and Monk, *loc. cit.*). In order to obtain the concentrations of the stock solutions of the salts, conductivity measurements were made with each one, and the concentrations found by interpolation from the known data.

I thank Dr. H. W. Jones for the trisethylenediaminocobalt(III) trimetaphosphate measurements, Messrs. Albright and Wilson for the sodium tetrametaphosphate, the Chemical Society for a grant for chemicals, and the Royal Society for a calculating machine.

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240. *Synthetic Analgesics and Related Compounds. Part IV.* Mannich Bases from Phenyl-substituted Acetones.*

By Walter Wilson and Zu-Yoong Kyi.

The series of Mannich bases (II; R′ = H), (VI), and (VII) have been obtained from 1 : 1-diphenylacetone, 1 : 3-diphenylacetone, and phenylacetone, respectively. The structure (II; R′ = H) was proved by degradation to the vinyl ketone (III) and to the methoxy-ketone (IV). The latter was not identical with the isomer (V) made by an unequivocal method. The bases (II; R′ = H) were unstable in neutral or alkaline solutions, and the vinyl ketone (III) appeared to be formed. Degradation of the bases (VII) afforded the αβ-unsaturated ketone (IX), which rapidly dimerised to the dihydropyran (X); the latter was also obtained as a by-product during the preparation of the bases (VII) from phenylacetone. The new bases are not analgesic, but several are potent local anæsthetics.

Few analogues of amidone, in which the side-chain length has been varied, are known; several δ- and ε-dialkylamino-ketones of this series had no analgesic activity (Dupré, Elks, Hems, Speyer, and Evans, *J.*, 1949, 500). It seemed possible that closely related bases (I) could be made from 1 : 1-diphenylacetone by the Mannich reaction; the products, however, were the isomers (II; R′ = H), as alkaline degradation of their quaternary salts gave the vinyl ketone (III). The structure of the latter was confirmed by the formation of a dibromide and by the intense light absorption at 210 mμ (ε > 23 000) (Fig. 2*c*); it was not identical with 4 : 4-diphenylbut-3-en-2-one (III*a*) (Klages and Fanto, *Ber.*, 1899, **32**, 1435), which could possibly arise from (I) by a carbonium-ion rearrangement (cf. Charlton, Dostrovsky, and Hughes, *Nature*, 1951, **167**, 986). The *cyclo*butanone structure (III*b*) was excluded as heating the ketone with aqueous sodium hydroxide gave a polymer and no carboxylic acid (cf. Bergmann and Blum-Bergmann, *J.*, 1938, 728). The methochloride of (II; R = Me, R′ = H) with methanolic sodium methoxide gave the methoxy-ketone (IV), which differed from the isomer (V) made by an unequivocal method (see below). These degradation experiments establish the structures (II; R′ = H) for the original bases, the Mannich reaction having taken place at position 3 of 1 : 1-diphenylacetone and not at position 1.† This result is not surprising, for although 1 : 1-diphenylacetone can be alkylated at position 1 (Tiffeneau and Levy, *Bull. Soc. chim.*, 1923, [4], **33**, 776; Part III), it condenses with benzaldehyde at position 3 (Staudinger and Rheiner, *Helv. Chim. Acta*, 1924, **7**, 15). Furthermore, 1-methyl-1 : 1-diphenylacetone readily forms Mannich bases (Zaugg, Freifelder, and Horrom, *J. Org. Chem.*, 1950, **15**, 1191), but diphenylmethyl phenyl ketone does not.

$CH_3{\cdot}CO{\cdot}CPh_2{\cdot}CH_2{\cdot}NR_2$ (I) $\quad$ $Ph_2CR'{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}NR_2$ (II)

$Ph_2CH{\cdot}CO{\cdot}CH{:}CH_2$ (III) $\quad$ $Ph_2C{:}CH{\cdot}CO{\cdot}CH_3$ (III*a*) $\quad$ $Ph_2\underline{C}{\cdot}CO{\cdot}CH_2{\cdot}\underline{C}H_2$ (III*b*)

$Ph_2CH{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}OMe$ (IV) $\quad$ $CH_3{\cdot}CO{\cdot}CPh_2{\cdot}CH_2{\cdot}OMe$ (V)

The ultra-violet absorption (Figs. 1*a* and 2*a*) of (II; R′ = H, R = Et) in acid solution indicated a 1 : 1-diphenylacetone structure (Kumler, Strait, and Alpen, *J. Amer. Chem. Soc.*, 1950, **72**, 1463), but the spectra do not appear to allow the 1- and the 3-substituted isomers to be differentiated. Very dilute solutions of the hydrochloride of (II; R = Et, R′ = H) soon developed intense absorption bands; this change was rapid in the presence of alkali (Fig. 2*b*) and is believed to be caused by partial conversion of the compound into (III), whose extinction curve is also given (Fig. 2*c*).

Contrary to Avison and Morrison's experience (*J.*, 1950, 1475) with benzyl ketones, no

* Part III, *J.*, 1952, 6.

† *Added in Proof.*—Protiva and Jílek (*Coll. Czech. Chem. Comm.*, 1951, **16**, 151) draw the same conclusion about the structures of the Mannich bases.

difficulty was experienced in making the series of Mannich bases (VI) and (VII) from 1 : 3-diphenylacetone and phenylacetone, respectively. It is possible that the anomalies encountered by these authors were due to the amine components used, as it is well known that certain amines undergo the Mannich reaction with difficulty (*e.g.*, "Org. Reactions," 1942, **1**, 307). Avison and Morrison prepared a Mannich base, shown to be (VII; NR_2 = $NMe{\cdot}CH_2{\cdot}CH{:}CH_2$), from phenylacetone. The bases now obtained from phenylacetone were also assigned the structure (VII), because they were convertible into the pyrazoline obtained by Avison and Morrison from their base, and the iodoform tests were positive.

FIG. 1.

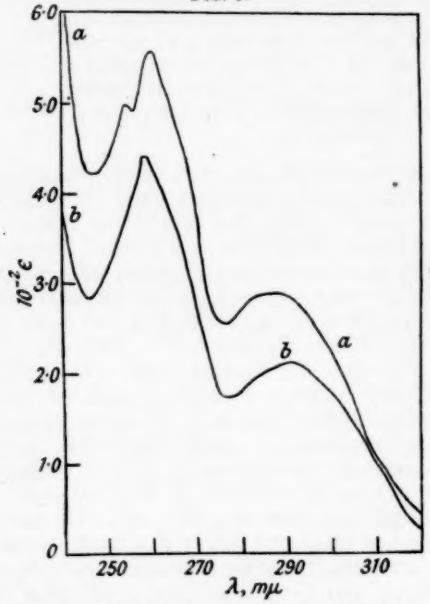


FIG. 2.

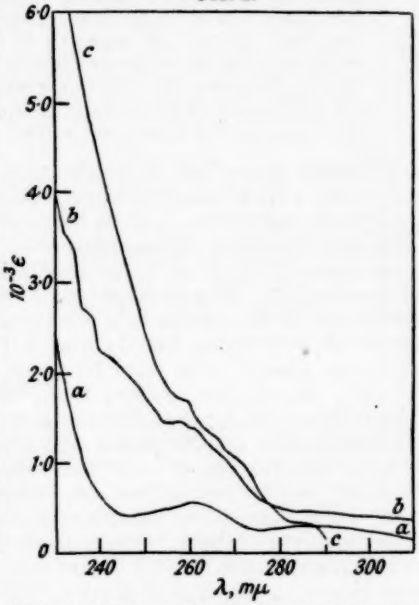


FIG. 1. a, 4-*Diethylamino*-1 : 1-*diphenylbutan*-2-*one hydrochloride in* N/100-*ethanolic hydrogen chloride.* $\lambda_{max.}$ (*mμ*) : 254 (ϵ = 498), 260 (ϵ = 558), 287 (ϵ = 280). $\lambda_{min.}$ (*mμ*) : 246 (ϵ = 422), 256 (ϵ = 491), 276 (ϵ = 257).

b, 4-*Methoxy*-3 : 3-*diphenylbutan*-2-*one in ethanol.* $\lambda_{max.}$ (*mμ*) : 258 (ϵ = 442), 290 (ϵ = 214). $\lambda_{min.}$ (*mμ*) : 246 (ϵ = 284), 276 (ϵ = 174).

FIG. 2. a, 4-*Diethylamino*-1 : 1-*diphenylbutan*-2-*one hydrochloride* (*details as for Fig.* 1, *curve* a).

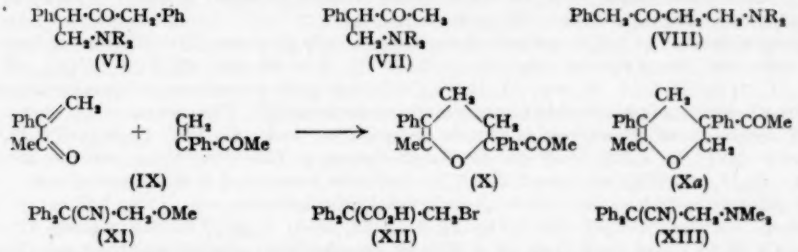
b, 4-*Diethylamino*-1 : 1-*diphenylbutan*-2-*one hydrochloride in ethanol* (75·2 *mg./l.*). *Solution set aside for* 24 *hours, then* N/10-*aqueous potassium hydroxide* (8 *c.c./l.*) *added, and spectrum measured immediately. Inflexion at* 258 *mμ* (ϵ = 1480).

c, 1 : 1-*Diphenylbut*-3-*en*-2-*one in ethanol.* $\lambda_{max.}$ (*mμ*) : 210 (ϵ > 23 000).

Aqueous alkali converted the methiodide of (VII; R = Me) into the αβ-unsaturated ketone (IX), which rapidly dimerised to the crystalline dihydropyran (X; or less probably X*a*). The same dihydropyran was formed (5—6%) as a by-product during the preparation of Mannich bases from phenylacetone. The dihydropyran structure was confirmed by the molecular weight, the formation of a mono-oxime, the positive iodoform reaction, and the presence of an inert (non-hydroxylic) oxygen atom. Analogous dimers have been obtained from αβ-unsaturated carbonyl compounds by Alder, Offermanns, and Rüden (*Ber.*, 1941, **74**, 926). It is probable that the compound $C_{18}H_{16}O_2$, m. p. 172°, obtained by alkaline degradation of 3-dimethylamino-1-phenylpropan-1-one methiodide (Jacob and Madinaveitia, *J.*, 1937, 1929) is similarly a dihydropyran formed by dimerisation of phenyl vinyl ketone.

Several unsuccessful attempts to synthesise β-dialkylamino-ketones by alternative

methods were made. Thus, diphenylmethyl cyanide and methoxymethyl bromide readily afforded the cyanide (XI), which yielded the methoxy-ketone (V) with methylmagnesium iodide. The methoxy-ketone could not be demethylated in boiling hydrobromic acid, but the required bromo-ketone may be obtainable from the corresponding acid (XII)



recently described (Zaugg, *J. Amer. Chem. Soc.*, 1950, **72**, 2998). Böckmuhl and Ehrhart (*Annalen*, 1948, **561**, 52) failed to ketonise the basic cyanide (XIII) in an attempt to make (I; R = Me). We failed to obtain ketonic products from 2-diethylaminoethyl cyanide and benzylmagnesium chloride (cf. Clarke and Mosher, *J. Amer. Chem. Soc.*, 1950, **72**, 1026).

The Mannich bases described were examined for biological activity in Dr. P. B. Marshall's laboratory (see acknowledgments). The compounds are not analgesic, but several are potent local anæsthetics. Thus (II; R′ = H, R = Me) and (VI; NR_2 = piperidino) are from 4 to 5 times as active as procaine on comparison by Bülbring and Wajda's method (*J. Pharmacol. Exper. Therap.*, 1945, **85**, 78), and their therapeutic indices are comparable with the value for cinchocaine B.P. These Mannich bases may be too unstable in solution for clinical use.

Experimental

4-Dimethylamino-1 : 1-diphenylbutan-2-one (II; R = Me, R′ = H).—A mixture of 1 : 1-diphenylacetone (105 g.), dimethylammonium chloride (65 g.), paraformaldehyde (24 g.), concentrated hydrochloric acid (3 c.c.), and ethanol (300 c.c.) was boiled under reflux for 16 hours. Excess of water was added and unreacted ketone (22 g., 21%) removed by ether extraction. The aqueous solution was made alkaline and the liberated base isolated by ether extraction. Treatment of the base with ethanolic hydrogen chloride gave the *hydrochloride* (76 g., 50% yield); this had m. p. 157—158° after recrystallisation from ethanol (Found: C, 70·9; H, 7·1; N, 4·8; Cl, 11·6. $C_{18}H_{21}ON,HCl$ requires C, 71·2; H, 7·25; N, 4·6; Cl, 11·7%). The iodoform test was negative as with 1 : 1-diphenylacetone. The *picrate* formed needles, m. p. 120—121°, from ethanol–ethyl acetate (Found: C, 57·8; H, 4·6. $C_{24}H_{24}O_8N_4$ requires C, 58·1; H, 4·8%), and the *methiodide* crystallised from ethanol as flakes, m. p. 145° (decomp.) (Found: C, 55·7; H, 6·1; I, 31·5. $C_{18}H_{21}ON,CH_3I$ requires C, 55·7; H, 5·9; I, 31·1%). The hydrochloride (45 g.) was converted into the base, which was dissolved in ethanol (250 c.c.) and saturated with gaseous methyl chloride; the somewhat impure *methochloride* (40 g., 85%) separated as needles, m. p. 145°, after being recrystallised from aqueous methanol (Found: C, 74·1; H, 7·0. $C_{19}H_{24}ONCl$ requires C, 71·8; H, 7·6%).

Slight modifications of the above procedure were used for making the following Mannich bases from the appropriate ketones and secondary amine hydrochlorides; in some cases (*A*) the hydrochlorides were isolated as above, in others (*B*) they crystallised out from the reaction mixture; the reaction times and the percentage yields are stated in each example.

4-Diethylamino-1 : 1-diphenylbutan-2-one hydrochloride (16 hours; *A*; 39%), m. p. 114—115° (Found: C, 72·3; H, 7·7; Cl, 10·55. $C_{20}H_{25}ON,HCl$ requires C, 72·4; H, 7·8; Cl, 10·7%); *picrate*, glistening flakes, m. p. 122—123° (from ethanol–ethyl acetate) (Found: C, 60·1; H, 5·3. $C_{20}H_{25}ON,C_6H_3O_7N_3$ requires C, 59·6; H, 5·3%).

1 : 1-Diphenyl-4-piperidinobutan-2-one hydrochloride (4 hours; *A*; 17%, with 72% of unreacted 1 : 1-diphenylacetone), m. p. 196—197° (from ethanol) (Found: C, 73·3; H, 7·2; N, 3·9; Cl, 10·1. $C_{21}H_{25}ON,HCl$ requires C, 73·35; H, 7·6; N, 4·1; Cl, 10·3%), was only slightly soluble in water. The *picrate* (from ethanol–ethyl acetate) had m. p. 150—151° (Found: C, 60·6; H, 5·4. $C_{21}H_{25}ON,C_6H_3O_7N_3$ requires C, 60·4; H, 5·2%).

4-*Morpholino*-1 : 1-*diphenylbutan*-2-*one hydrochloride* (16 hours; *A*; 49%, with 46% of unreacted ketone), m. p. 183—184° (Found : Cl, 10·3. $C_{20}H_{23}O_2N,HCl$ requires Cl, 10·3%), was very sparingly soluble in water and ethanol. The *picrate* formed needles, m. p. 139—140°, from ethanol–ethyl acetate (Found : C, 57·9; H, 5·0. $C_{20}H_{23}O_2N,C_6H_3O_7N_3$ requires C, 58·0; H, 4·8%); the *methiodide* had m. p. 137—138° (from ethanol) (Found : C, 55·3; H, 5·4; I, 28·4. $C_{20}H_{23}O_2N,CH_3I$ requires C, 55·9; H, 5·8; I, 28·2%).

4-*Dimethylamino*-1 : 3-*diphenylbutan*-2-*one hydrochloride* (4 hours; *B*; 57%) formed needles, m. p. 163—164°, from ethanol (Found : C, 71·1; H, 7·3; N, 4·8; Cl, 11·6. $C_{18}H_{21}ON,HCl$ requires C, 71·2; H, 7·25; N, 4·6; Cl, 11·7%). Doubling the proportions of paraformaldehyde and dimethylammonium chloride increased the yield to 77%. The *picrate*, m. p. 105—106°, formed needles from ethanol–ethyl acetate (Found : C, 58·1; H, 4·8. $C_{18}H_{21}ON,C_6H_3O_7N_3$ requires C, 58·1; H, 4·8%), and the *methiodide* had m. p. 129—130° (from acetone) (Found : I, 31·4. $C_{18}H_{21}ON,CH_3I$ requires I, 31·1%); the latter compound slowly decomposed.

4-*Diethylamino*-1 : 3-*diphenylbutan*-2-*one hydrochloride* (4 hours; *A*; 13%) had m. p. 115—116° (from acetone) (Found : C, 72·1; H, 7·5; Cl, 10·5. $C_{20}H_{25}ON,HCl$ requires C, 72·4; H, 7·8; Cl, 10·7%), and the *picrate*, m. p. 97—98° (needles from ethanol–ethyl acetate) (Found : C, 59·7; H, 5·3. $C_{20}H_{25}ON,C_6H_3O_7N_3$ requires C, 59·55; H, 5·3%).

1 : 3-*Diphenyl*-4-*piperidinobutan*-2-*one hydrochloride* (4 hours; *B*; 30%) formed sparingly soluble needles, m. p. 162—163°, from ethanol (Found : C, 73·1; H, 7·3; N, 4·3; Cl, 10·3. $C_{21}H_{25}ON,HCl$ requires C, 73·35; H, 7·6; N, 4·1; Cl, 10·3%). The *base*, recrystallised from ethyl acetate–light petroleum (b. p. 60—80°), had m. p. 71—71·5° (Found : C, 82·5; H, 7·6. $C_{21}H_{25}ON$ requires C, 82·1; H, 8·1%), and the *picrate* formed prisms, m. p. 116—117° (from 80% ethanol) (Found : C, 60·6; H, 5·0. $C_{21}H_{25}ON,C_6H_3O_7N_3$ requires C, 60·4; H, 5·2%).

4-*Morpholino*-1 : 3-*diphenylbutan*-2-*one hydrochloride* (4 hours; *B*; 59%) crystallised from 80% methanol as cubes, m. p. 170—171° (Found : Cl, 10·2. $C_{20}H_{23}O_2N,HCl$ requires Cl, 10·3%). The *base* formed needles, m. p. 75—75·5°, from ethyl acetate–light petroleum (b. p. 60—80°) (Found : C, 77·4; H, 7·4. $C_{20}H_{23}O_2N$ requires C, 77·65; H, 7·45%), and the *picrate*, flakes, m. p. 155·5—156°, from 80% methanol (Found : C, 57·8; H, 4·6. $C_{20}H_{23}O_2N,C_6H_3O_7N_3$ requires C, 58·0; H, 4·8%).

4-*Dimethylamino*-3-*phenylbutan*-2-*one hydrochloride* (4 hours; *B*; 61%) formed colourless cubes, m. p. 155—156°, from *iso*propanol (Found : C, 63·3; H, 7·9; N, 6·0; Cl, 15·5. $C_{12}H_{17}ON,HCl$ requires C, 63·3; H, 7·9; N, 6·15; Cl, 15·6%); the iodoform test was positive. Treatment with sodium hydroxide afforded the *base*, b. p. 91—93°/0·05 mm. (Found : C, 75·8; H, 8·7; N, 7·0. $C_{12}H_{17}ON$ requires C, 75·4; H, 8·9; N, 7·3%), which slowly evolved dimethylamine. The *picrate* formed needles, m. p. 98—99°, from ethanol–ethyl acetate (Found : C, 51·6; H, 4·9. $C_{12}H_{17}ON,C_6H_3O_7N_3$ requires C, 51·4; H, 4·8%), and the *methiodide* had m. p. 190—191° from water (Found : C, 46·5; H, 5·8; N, 4·3; I, 38·0. $C_{12}H_{17}ON,CH_3I$ requires C, 46·8; H, 6·0; N, 4·2; I, 38·15%).

4-*Diethylamino*-3-*phenylbutan*-2-*one hydrochloride* (4 hours; *A*; 22%) had m. p. 123·5—124·5° (from acetone–ethanol) (Found : C, 65·8; H, 8·4; Cl, 13·9. $C_{14}H_{21}ON,HCl$ requires C, 65·75; H, 8·6; Cl, 13·9%); the *picrate* had m. p. 78·5—79·5° (prisms from ethanol) (Found : C, 54·0; H, 5·3. $C_{14}H_{21}ON,C_6H_3O_7N_3$ requires C, 53·6; H, 5·35%) and the *methiodide* m. p. 113—114° (from *iso*propanol) (Found : C, 49·6; H, 6·7. $C_{14}H_{21}ON,CH_3I$ requires C, 49·9; H, 6·65%).

3-*Phenyl*-4-*piperidinobutan*-2-*one hydrochloride* (4 hours; *B*; 52%) formed colourless cubes, m. p. 157—158°, from acetone–ethanol (Found : C, 67·2; H, 8·0; N, 5·5; Cl, 13·2. $C_{15}H_{21}ON,HCl$ requires C, 67·3; H, 8·2; N, 5·2; Cl, 13·3%). The *base*, m. p. 40·5—41°, was recrystallised from ethyl acetate–light petroleum (b. p. 60—80°) (Found : C, 77·4; H, 8·7. $C_{15}H_{21}ON$ requires C, 77·9; H, 9·1%); the *picrate* had m. p. 107—108° (glistening flakes from ethanol) (Found : C, 54·6; H, 4·9. $C_{15}H_{21}ON,C_6H_3O_7N_3$ requires C, 54·8; H, 5·2%) and the *methiodide* m. p. 152—153° (from acetone–ethanol) (Found : C, 51·5; H, 6·4; I, 34·1. $C_{15}H_{21}ON,CH_3I$ requires C, 51·5; H, 6·4; I, 34·05%).

4-*Morpholino*-3-*phenylbutan*-2-*one hydrochloride* (4 hours; *B*; 70%) crystallised in cubes, m. p. 175—176°, from 80% methanol (Found : Cl, 13·0. $C_{14}H_{19}O_2N,HCl$ requires Cl, 13·2%). The *base*, crystallised from ethyl acetate–light petroleum (b. p. 60—80°), had m. p. 51—52° (Found : C, 72·1; H, 8·1. $C_{14}H_{19}O_2N$ requires C, 72·1; H, 8·2%), the *picrate* m. p. 119—120° (prisms from ethanol) (Found : C, 51·95; H, 4·8. $C_{14}H_{19}O_2N,C_6H_3O_7N_3$ requires C, 51·9; H, 4·8%), and the *perchlorate* m. p. 151—152° (needles from ethanol) (Found : C, 50·8; H, 5·8. $C_{14}H_{19}O_2N,HClO_4$ requires C, 50·4; H, 6·0%).

Degradation of 4-*Dimethylamino*-1 : 1-*diphenylbutan*-2-*one Methochloride.*—(a) *With sodium*

hydroxide. The methochloride (20 g.) was stirred with sodium hydroxide (10 g.) in water (300 c.c.) for 1 hour at 25°. Extraction with benzene and distillation afforded 1 : 1-*diphenylbut*-3-*en*-2-*one* (III) (6 g., 43% yield), b. p. 103—105°/0·01 mm., which gave crystals, m. p. 53—54°, from light petroleum (b. p. 60—80°) containing a little ethyl acetate (Found : C, 86·9; H, 6·4. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). Hot concentrated sodium hydroxide polymerised this compound to a brittle glass. The ketone (0·5 g.) with a slight excess of bromine in chloroform at 30—35° afforded 3 : 4-*dibromo*-1 : 1-*diphenylbutan*-2-*one* (0·79 g., 92%), which formed needles, m. p. 79—80°, from light petroleum (b. p. 60—80°) (Found : C, 50·3; H, 3·9; Br, 41·9. $C_{16}H_{14}OBr_2$ requires C, 50·25; H, 3·7; Br, 41·9%).

(b) *With sodium methoxide.* The methochloride (5 g.) was dissolved in a mixture of methanol (100 c.c.) and benzene (30 c.c.), and a cold solution of sodium methoxide [from sodium (0·7 g.) and methanol (40 c.c.)] was added. After 90 minutes the mixture was poured into 3N-hydrochloric acid (200 c.c.), and the acid mixture extracted with benzene. Distillation of the extract afforded 4-*methoxy*-1 : 1-*diphenylbutan*-2-*one* (IV) (1·9 g., 47%), b. p. 120—122°/0·05 mm.; n_D^{22} 1·5611 (Found : C, 80·3; H, 7·1. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). The *oxime* had m. p. 97—98° (Found : C, 76·5; H, 7·15. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1%); a mixture with 4 : 4-diphenylbut-3-en-2-one oxime had a much lower melting point.

4 : 4-*Diphenylbut*-3-*en*-2-*one* (III*a*).—(Cf. Klages and Fanto, *Ber.*, 1899, **32**, 1435.) Redistilled diphenyldichloromethane (24 g.) was boiled for 6 hours with a suspension of dry cupric acetoacetate (32 g.) in absolute ethanol (50 c.c.). The mixture was diluted with ether and filtered, and the filtrate washed with dilute aqueous sodium hydroxide. Distillation afforded crude ethyl α-acetyl-ββ-diphenylacrylate (14·4 g.), b. p. 157—167°/0·02 mm., which solidified. The crude ester was boiled for 6 hours with potassium hydroxide (7 g.) in aqueous ethanol (35 c.c.). The alcohol was distilled off and neutral substances removed by ether extraction. Addition of hydrochloric acid precipitated α-acetyl-ββ-diphenylacrylic acid as an oil, which was isolated by extraction with benzene. The crude acid (10·5 g.) was heated at 15 mm. pressure; violent effervescence occurred, then a mobile oil (6·0 g.) distilled at 195—205°/15 mm. Redistillation gave 4 : 4-diphenylbut-3-en-2-one, b. p. 140°/0·015 mm.; n_D^{25} 1·6165, which gave an oxime, m. p. 92·5—94°, and a 2 : 4-*dinitrophenylhydrazone*, which formed bright red prisms, m. p. 153—154°, from ethanol (Found : N, 14·3. $C_{22}H_{18}O_4N_4$ requires N, 14·0%).

Degradation of 4-*Morpholino*-1 : 1-*diphenylbutan*-2-*one Methiodide.*—The methiodide (10 g.) was heated for 1 hour at 40—50° with 10% aqueous sodium hydroxide (100 c.c.). The oil was extracted with ether, and the ether layer shaken with excess of dilute hydrochloric acid. The crystals (4·4 g., 58%) which separated were 4-morpholino-1 : 1-diphenylbutan-2-one hydrochloride. The ethereal filtrate was washed with aqueous sodium hydrogen carbonate, dried, and distilled, affording 1 : 1-diphenylbut-3-en-2-one (0·9 g., 18%), b. p. 110—118°/0·04 mm., m. p. 53—54° after recrystallisation from light petroleum (b. p. 60—80°). The methiodide did not appear to react with 3% sodium hydroxide solution at 20°.

2-*Acetyl*-2 : 3-*dihydro*-6-*methyl*-2 : 5-*diphenylpyran* (X).—(a) *From the preparation of* 4-*dimethylamino*-3-*phenylbutan*-2-*one hydrochloride.* The liquors from which the hydrochloride had crystallised were diluted with excess of water and extracted with ether. The fraction of b. p. 130—140°/0·5 mm. was crystallised from aqueous methanol, and gave the *dihydropyran* (1·7 g., 6% yield) as white needles, m. p. 78—79° [Found : C, 82·7; H, 6·85%; *M* (Rast), 252. $C_{20}H_{20}O_2$ requires C, 82·2; H, 6·85%; *M*, 292]; ultra-violet extinction maximum at 247 mμ ($E_{1\,cm.}^{1\%}$ 247) in ethanol solution. The iodoform test (Fuson and Tullock's modification, *J. Amer. Chem. Soc.*, 1934, **56**, 1638) was strongly positive, and a solution of bromine in chloroform was decolorised rapidly in the cold with evolution of hydrogen bromide. The compound did not react with acetic anhydride in pyridine, and the *oxime*, prepared in 70% ethanol, formed prisms, m. p. 153° (Found : C, 78·5; H, 6·9; N, 4·8. $C_{20}H_{21}O_2N$ requires C, 78·2; H, 6·85; N, 4·6%).

(b) *By degradation of* 4-*dimethylamino*-3-*phenylbutan*-2-*one methiodide.* The methiodide (28 g.) was stirred with 3% aqueous sodium hydroxide (300 c.c.) at 20°. The oil which separated was extracted with benzene and distilled, giving 3-phenylbut-3-en-2-one (8·5 g., 69%), b. p. 54—55°/0·8 mm. This dimerised, before it could be analysed, to the solid dihydropyran (X), b. p. 133—136°/0·8 mm., m. p. 76—77° after recrystallisation from light petroleum (b. p. 60—80°) [Found : C, 82·0; H, 6·8. Calc. for $(C_{10}H_{10}O)_n$: C, 82·2; H, 6·85%]. The oxime had m. p. 154·5—155·5°, not depressed on admixture of the sample with the oxime obtained in (*a*).

3-*Methyl*-1 : 4-*diphenylpyrazoline.*—4-Dimethylamino-3-phenylbutan-2-one hydrochloride (3 g.), sodium acetate (3 g.), and phenylhydrazine (3 g.) were dissolved in a mixture of ethanol

(10 c.c.) and glacial acetic acid (10 c.c.), and the sodium chloride filtered off. The solution was boiled for 6 hours; the resulting pyrazoline formed pale yellow plates, m. p. 159—160°, from methanol (Avison and Morrison, *J.*, 1950, 1474, give m. p. 159—160°). The same pyrazoline was obtained from the other Mannich bases derived from phenylacetone.

2-Methoxy-1 : 1-diphenylethyl Cyanide (XI).—Diphenylmethyl cyanide (97 g.) was stirred at 30—35° with powdered sodamide (31 g.) in dry benzene (300 c.c.). Methoxymethyl bromide (87·5 g.) (Vavon, Bolle, and Calin, *Bull. Soc. chim.*, 1939, [5], **6**, 1032) in dry benzene (70 c.c.) was added slowly with cooling to 45—50°. The mixture was refluxed for 2 hours, then washed with water, and distilled. The fraction of b. p. 148—152°/0·1 mm. (73 g.) was recrystallised from *iso*propanol, yielding *2-methoxy-1 : 1-diphenylethyl cyanide* (48 g., 41%), m. p. 56—57° (Found: C, 81·0; H, 6·5. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·3%).

4-Methoxy-3 : 3-diphenylbutan-2-one (V).—The cyanide (XI) (35·6 g.) in toluene (80 c.c.) was mixed with a Grignard solution from magnesium (3·8 g.), methyl iodide (25 g.), and ether (60 c.c.). The ether was distilled off and the residual solution refluxed for 3 hours. Water (80 c.c.) and concentrated hydrochloric acid (50 c.c.) were added and the toluene layer separated and distilled. The fraction of b. p. 131—135°/0·1 mm. solidified and was recrystallised from methanol, affording the *methoxy-ketone* (14 g., 73%) as needles, m. p. 92·5—93·5° (Found: C, 80·4; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). The compound did not appear to be demethylated by boiling 48% hydrobromic acid. The *oxime* was obtained by heating the ketone for 3 hours with hydroxylamine hydrochloride and sodium acetate in ethanol, and had m. p. 167—168° (Found: C, 76·1; H, 7·2. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1%).

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241. *Densities of Some Binary Liquid Mixtures. Part I.*

By V. S. GRIFFITHS.

Densities at 25° of binary mixtures of water with dioxan, acetone, and pyridine, and of mixtures of ethanol and pyridine are reported.

FOR other work it was necessary to know accurately the densities of various binary mixtures over the complete concentration range. Such determinations had been made by other workers but, in general, agreement was poor and seldom was the range 0—100% adequately covered. The system dioxan–water from 35 to 100% of dioxan was investigated by Hovorka, Schaefer, and Dreisbach (*J. Amer. Chem. Soc.*, 1936, **58**, 2264); Geddes (*ibid.*, 1933, **55**, 4832), who covered a greater concentration range but in less detail, reported a minimum in the concentration–density curve at approximately 1% of water.

Aqueous solutions of pyridine were studied by Hartley, Thomas, and Applebey (*J.*, 1908, **93**, 538) and Dunstan, Thole, and Hunt (*J.*, 1907, **91**, 1728; 1908, **93**, 561). The latter authors also published densities of ethanolic solutions of pyridine (*loc. cit.*), and later work is reported by Hatem (*Bull. Soc. chim.*, 1949, **16**, 599).

Tabulated data for the acetone–water system at 25° were scarce, but two sets of figures were available at 20°, *viz.*, those of Naville (*Helv. Chim. Acta*, 1926, **9**, 913) and of Young (*J. Soc. Chem. Ind.*, 1933, **52**, 449). According to the International Critical Tables (1929) the densities of aqueous solutions of acetone can be calculated from the formula

$$d = d_w - 1{\cdot}171 \times 10^{-3}p_s - 9{\cdot}04 \times 10^{-6}p_s^2 - 5{\cdot}6 \times 10^{-9}p_s^3$$

where d = density of solution, d_w = density of water, and p_s = weight concentration of acetone.

For aqueous pyridine at 25·08°, Hartley, Thomas, and Applebey reported a continous variation of density with concentration, whereas Dunstan, Thole, and Hunt's results were

best represented by a series of discontinuous curves. Hartley *et al.* pointed out that, if the law of mass action holds, it is not possible for a homogeneous liquid mixture to show a discontinuous change of density with composition at constant temperature and pressure, unless there is a sudden change in the equilibrium constant of one of the systems.

The published data for ethanolic solutions of pyridine showed considerable discrepancies, and marked discontinuities in the concentration–density curves were reported.

It thus seemed desirable to carry out a complete investigation of these systems. All measurements were made at 25° ± 0·005°, and the values of d quoted in the following tables are with reference to water at 4°.

Two types of pyknometer of volumes between 10 and 25 c.c. were used, one being the conventional Sprengel type (see Partington, "An Advanced Treatise on Physical Chemistry," Vol. II, 1951, Longmans), the other based on a suggestion by D. I. Stock (private communication). The latter was simple in design, consisting essentially of two parallel vertical capillary tubes of unequal length, their lower ends being connected by a

1 : 4-*Dioxan–water mixtures.*

$C_4H_8O_2$, % (w/w)	d	Mean	$C_4H_8O_2$, % (w/w)	d	Mean	$C_4H_8O_2$, % (w/w)	d	Mean
0	0·99706		50·37	1·03261		90·72	1·02943	
	0·99705	0·99706		1·03255	1·03258		1·02937	1·02940
11·21	1·00605		59·96	1·03602		95·28	1·02840	
	1·00599	1·00602		1·03613	1·03607		1·02848	1·02844
20·10	1·01360		66·42	1·03702		99·06	1·02820	
	1·01370	1·01365		1·03694	1·03698		1·02812	1·02816
30·07	1·02105		69·82	1·03703		100·00	1·02806	
	1·02101	1·02103		1·03696	1·03700		1·02810	1·02808
39·68	1·02704		80·02	1·03490				
	1·02695	1·02700		1·03494	1·03492			

Pyridine–water mixtures.

C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean
0	0·99707		35·58	1·00257		75·06	0·99967	
	0·99705	0·99706		1·00248	1·00253		0·99959	0·99963
5·07	0·99838		42·00	1·00281		82·03	0·99616	
	0·99833	0·99836		1·00280	1·00281		0·99605	0·99611
10·13	0·99937		50·21	1·00329		86·02	0·99307	
	0·99931	0·99938		1·00322	1·00326		0·99310	0·99309
19·86	1·00019		57·46	1·00311		89·38	0·98971	
	1·00014	1·00017		1·00303	1·00307		0·98979	0·98975
25·54	1·00166		59·38	1·00282		94·08	0·98467	
	1·00156	1·00161		1·00277	1·00280		0·98458	0·98463
30·05	1·00207		66·49	1·00208		100·00	0·97803	
	1·00201	1·00204		1·00216	1·00212		0·97797	0·97800

Pyridine-ethanol mixtures.

C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean
0	0·78506		41·78	0·87214		80·07	0·94430	
	0·78510	0·78508		0·87205	0·87210		0·94422	0·94426
10·10	0·80444		50·06	0·88804		88·75	0·95957	
	0·80440	0·80442		0·88810	0·88807		0·95949	0·95953
20·93	0·82754		62·03	0·91186		100·00	0·97803	
	0·82748	0·82751		0·91178	0·91182		0·97797	0·97800
29·67	0·84713		69·11	0·92907				
	0·84705	0·84709		0·92898	0·92903			

Acetone-water mixtures.

$COMe_2$, % (w/w)	d	Mean	$COMe_2$, % (w/w)	d	Mean	$COMe_2$, % (w/w)	d	Mean
0	0·99706		39·98	0·93726		80·74	0·84210	
	0·99705	0·99706		0·93722	0·93724		0·84219	0·84205
9·82	0·98571		51·43	0·91406		89·15	0·81875	
	0·98574	0·98573		0·91398	0·91402		0·81864	0·81872
21·23	0·96937		60·49	0·89369		100·0	0·78512	
	0·96941	0·96939		0·89364	0·89367		0·78502	0·78507
29·62	0·95616		71·89	0·86582				
	0·95605	0·95611		0·86574	0·86578			

cylindrical bulb. The upper ends of the tubes were fitted with ground-glass caps and were at the same horizontal height so that the bulb was at an angle to both limbs. It was found that, if the apparatus was filled in the inverted position through the shorter limb no troublesome "air-locks" occurred. Most of the observations were made in duplicate with the latter type of pyknometer.

Discussion.—The data for the dioxan solutions agree well with those of Hovorka *et al.* and extend the work below 35% of dioxan. The minimum at 1% of water reported by Geddes was not found.

The results for the pyridine–water mixtures lie on a smooth curve and agree well with those of Hartley, Thomas, and Applebey, the temperature difference being taken into account.

Ethanolic solutions of pyridine proved to be the most difficult to investigate, as both liquids are very hygroscopic. A blank series of estimations showed variations of 4 and 5 units in the fourth place of decimals after solutions had been exposed to the atmosphere for 10 minutes. The results indicate that the density varies continuously with concentration.

The densities for aqueous solutions of acetone differed considerably from those given by the formula above. The results were plotted on a large scale, and the best curve was drawn. A set of simultaneous equations derived from points on this curve were solved to give a new equation:

$$d = 0{\cdot}99706 - 1{\cdot}091 \times 10^{-3}p_s - 9{\cdot}93 \times 10^{-6}p_s^2 - 3{\cdot}52 \times 10^{-9}p_s^3$$

The maximum difference between the experimental and calculated results was 0·0003.

Experimental

The organic solvent was distilled in all-glass apparatus directly into a roughly calibrated flask containing a known weight of conductivity water or alcohol under nitrogen. When the approximately correct volume had been collected the flask was re-weighed. The mixed solvent was transferred to the pyknometers either by blowing it over from the collecting flask through all-glass apparatus by means of dry nitrogen, or by "sucking" it over under reduced pressure.

The pyknometers were kept at 25° ± 0·005° and later weighed. All weighings were corrected to the vacuum standard and buoyancy corrections were made.

Owing to their hygroscopic nature, particular care was necessary when dealing with the organic solvents, and the pyknometers were kept stoppered or protected by drying tubes.

Materials.—The organic liquids were fractionally distilled at some stage in their purification and for this purpose 20-plate all-glass distillation columns were used (see Few and Smith, *J.*, 1949, 753).

Commercial 1 : 4-dioxan was fractionally distilled, and the middle fraction purified by repeated refluxing with sodium and fractional distillations (Kraus and Vingee, *J. Amer. Chem. Soc.*, 1934, **56**, 513), interposed with fractional crystallisations; the product had b. p. 101·40°/760 mm.

Commercial acetone was fractionally distilled and treated by Shipsey and Werner's method (*J.*, 1913, **103**, 1255) as modified by Livingston (*J. Amer. Chem. Soc.*, 1947, **69**, 1220). The product was refluxed with potassium permanganate, dried (K_2CO_3), and distilled in a stream of dry nitrogen; it had b. p. 56·20°/760 mm.

Pyridine (commercial) was distilled, and the 113—116° fraction repeatedly refluxed with potassium permanganate and sodium hydroxide until the solution retained its characteristic colour. The product was then fractionally distilled in a stream of dry nitrogen and dried over ignited barium oxide; it had b. p. 114·48°/760 mm.

Ethanol (99%) was treated by Donner and Hildebrand's method (*J. Amer. Chem. Soc.*, 1922, **44**, 2824) for the removal of aldehydes and heated under reflux over fresh lime. The product was boiled with anhydrous copper sulphate whilst a stream of nitrogen was passed through it, and finally redistilled over amalgamated aluminium chippings; it had b. p. 78·30°/760 mm.

All solvents were stored under nitrogen in sealed glass containers and redistilled in a stream of nitrogen immediately before use.

The water used in the mixtures was good-quality conductivity water.

Battersea Polytechnic, London, S.W.11. [*Received, November 20th*, 1951.]

242. *Preparation of Optically Active Lysine labelled with* ^{14}C *and* ^{15}N.

By H. R. V. Arnstein, G. D. Hunter, H. M. Muir, and A. Neuberger.

Syntheses of [*carboxy*-^{14}C], [α-^{14}C], and [α-^{15}N]lysine are described. The attempted separation of the [α-^{14}C]-labelled enantiomorphs by addition of optically active carrier lysine was not completely successful owing to extensive coprecipitation, which was demonstrated by an enzymic assay of the products. The L-[α-^{15}N]lysine was prepared in 90% yield from $^{15}NH_3$ by utilizing the inversion of configuration which occurs when the D-bromo-acid is treated with ammonia.

For metabolic studies to be reported elsewhere, we required L-lysine labelled with ^{14}C at the α- and the carboxyl-carbon atom severally and with ^{15}N as one of the two nitrogen atoms. Various syntheses of labelled lysine have been reported in the American literature. Thus, Weissman and Schoenheimer (*J. Biol. Chem.*, 1941, **140**, 779) utilizing the method of Eck and Marvel (*ibid.*, 1934, **106**, 387) obtained this amino-acid labelled with deuterium and ^{15}N in the α-position. DL-Lysine containing ^{15}N in the ε-position was prepared by condensation of labelled potassium phthalimide with ethyl 6-bromo-2-carbethoxy-2-phthalimidohexanoate * (Fink, Enns, Kimball, Silberstein, Bale, Madden, and Whipple, *J. Exp. Med.*, 1944, **80**, 455). Recently two groups of workers utilized the method of Fischer and Weigert (*Ber.*, 1902, **35**, 3772) for the preparation of lysine labelled with ^{14}C in the ε-position (Olynyk, Camp, Griffith, Woislowski, and Helmkamp, *J. Org. Chem.*, 1948, **13**, 465; Borsook, Deasy, Haagen-Smit, Keighley, and Lowy, *J. Biol. Chem.*, 1948, **176**, 1383).

In isotope work it is desirable to introduce the labelled atom at the latest possible stage of the synthesis. None of the methods described above was therefore thought suitable for our purpose and this also applies to various synthesis of lysine recently reported (Warner and Moe, *J. Amer. Chem. Soc.*, 1948, **70**, 3918; Degering and Boatright, *ibid.*, 1950, **72**, 5137; Gagnon and Boivin, *Canad. J. Res.*, 1948, **26**, *B*, 503). In the present work DL-[*carboxy*-^{14}C]lysine was obtained by an adaptation of Adamson's synthesis (*J.*, 1939, 1564). Methyl 2-keto*cyclo*hexane-1-[^{14}C]carboxylate was prepared by carboxylation of the sodium derivative of *cyclo*hexanone with [^{14}C]carbon dioxide, the procedure being a modification of that used by Levine and Hauser (*J. Amer. Chem. Soc.*, 1944, **66**, 1768). It was then treated with hydrazoic acid in chloroform in the presence of dry hydrogen chloride under the conditions used by Adamson (*loc. cit.*) for the corresponding ethyl ester. Hydrolysis with hydrochloric acid gave α-aminopimelic acid from which was obtained, under the usual conditions of the Schmidt reaction, lysine which was isolated as the dipicrate. This was converted into DL-lysine monohydrochloride on which all radioactive assays were carried out. The net yield of [*carboxy*-^{14}C]lysine was 12·2%, based upon the barium [^{14}C]carbonate used. An adaptation of Gaudry's synthesis (*Canad. J. Res.*, 1948, **26**, *B*, 387) to small-scale work for the synthesis of [*carboxy*-^{14}C]lysine has been reported by Borsook, Deasy, Haagen-Smit, Keighley, and Lowy (*J. Biol. Chem.*, 1950, **184**, 529): the yield stated was similar (10—15%), but the method is based on the more expensive sodium [^{14}C]cyanide.

DL-Lysine labelled with ^{14}C at the α-carbon atom was synthesized as follows: 4-Chlorobutan-1-ol, obtained from tetrahydrofuran (Starr and Hixon, *J. Amer. Chem. Soc.*, 1934, **56**, 1595), was converted into the chloro-bromide by an adaptation of the method of Cloke, Anderson, Lachmann, and Smith (*ibid.*, 1931, **53**, 2791). The chloro-bromide in slight excess was then caused to react with potassium phthalimide to give, apart from the desired *n*-chlorobutylphthalimide, some 1 : 4-diphthalimidobutane. The chloro-compound on treatment with sodium iodide in acetone yielded 4-iodobutylphthalimide. The latter was condensed with ethyl phthalimido[α-^{14}C]malonate, prepared from ethyl [α-^{14}C]malonate (*Org. Synth.*, 1927, **7**, 34, 78). The condensation product which was not isolated was heated under reflux with a mixture of hydrochloric and acetic acids. A somewhat similar

* Geneva nomenclature, $CO_2H = 1$.

(10 c.c.) and glacial acetic acid (10 c.c.), and the sodium chloride filtered off. The solution was boiled for 6 hours; the resulting pyrazoline formed pale yellow plates, m. p. 159—160°, from methanol (Avison and Morrison, *J.*, 1950, **1474**, give m. p. 159—160°). The same pyrazoline was obtained from the other Mannich bases derived from phenylacetone.

2-Methoxy-1 : 1-diphenylethyl Cyanide (XI).—Diphenylmethyl cyanide (97 g.) was stirred at 30—35° with powdered sodamide (31 g.) in dry benzene (300 c.c.). Methoxymethyl bromide (87·5 g.) (Vavon, Bolle, and Calin, *Bull. Soc. chim.*, 1939, [5], **6**, 1032) in dry benzene (70 c.c.) was added slowly with cooling to 45—50°. The mixture was refluxed for 2 hours, then washed with water, and distilled. The fraction of b. p. 148—152°/0·1 mm. (73 g.) was recrystallised from *iso*propanol, yielding *2-methoxy-1 : 1-diphenylethyl cyanide* (48 g., 41%), m. p. 56—57° (Found: C, 81·0; H, 6·5. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·3%).

4-Methoxy-3 : 3-diphenylbutan-2-one (V).—The cyanide (XI) (35·6 g.) in toluene (80 c.c.) was mixed with a Grignard solution from magnesium (3·8 g.), methyl iodide (25 g.), and ether (60 c.c.). The ether was distilled off and the residual solution refluxed for 3 hours. Water (80 c.c.) and concentrated hydrochloric acid (50 c.c.) were added and the toluene layer separated and distilled. The fraction of b. p. 131—135°/0·1 mm. solidified and was recrystallised from methanol, affording the *methoxy-ketone* (14 g., 73%) as needles, m. p. 92·5—93·5° (Found: C, 80·4; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). The compound did not appear to be demethylated by boiling 48% hydrobromic acid. The *oxime* was obtained by heating the ketone for 3 hours with hydroxylamine hydrochloride and sodium acetate in ethanol, and had m. p. 167—168° (Found: C, 76·1; H, 7·2. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1%).

The authors are grateful to Professor M. Stacey, F.R.S., for encouragement and for facilities; they are also indebted to Mr. B. Stringer for most of the microanalyses, and to Dr. P. B. Marshall, Miss R. E. Weston, and Dr. Nazeer ud din Ahmad of the Department of Pharmacology for the bioassays, details of which are being published elsewhere. Most of this work was carried out during the tenure by one of us (Z.-Y. K.) of a scholarship from the Sino-British Educational and Cultural Endowment Fund.

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241. *Densities of Some Binary Liquid Mixtures. Part I.*

By V. S. GRIFFITHS.

Densities at 25° of binary mixtures of water with dioxan, acetone, and pyridine, and of mixtures of ethanol and pyridine are reported.

FOR other work it was necessary to know accurately the densities of various binary mixtures over the complete concentration range. Such determinations had been made by other workers but, in general, agreement was poor and seldom was the range 0—100% adequately covered. The system dioxan–water from 35 to 100% of dioxan was investigated by Hovorka, Schaefer, and Dreisbach (*J. Amer. Chem. Soc.*, 1936, **58**, 2264); Geddes (*ibid.*, 1933, **55**, 4832), who covered a greater concentration range but in less detail, reported a minimum in the concentration–density curve at approximately 1% of water.

Aqueous solutions of pyridine were studied by Hartley, Thomas, and Applebey (*J.*, 1908, **93**, 538) and Dunstan, Thole, and Hunt (*J.*, 1907, **91**, 1728; 1908, **93**, 561). The latter authors also published densities of ethanolic solutions of pyridine (*loc. cit.*), and later work is reported by Hatem (*Bull. Soc. chim.*, 1949, **16**, 599).

Tabulated data for the acetone–water system at 25° were scarce, but two sets of figures were available at 20°, *viz.*, those of Naville (*Helv. Chim. Acta*, 1926, **9**, 913) and of Young (*J. Soc. Chem. Ind.*, 1933, **52**, 449). According to the International Critical Tables (1929) the densities of aqueous solutions of acetone can be calculated from the formula

$$d = d_w - 1{\cdot}171 \times 10^{-3}p_s - 9{\cdot}04 \times 10^{-6}p_s^2 - 5{\cdot}6 \times 10^{-9}p_s^3$$

where d = density of solution, d_w = density of water, and p_s = weight concentration of acetone.

For aqueous pyridine at 25·08°, Hartley, Thomas, and Applebey reported a continous variation of density with concentration, whereas Dunstan, Thole, and Hunt's results were

best represented by a series of discontinuous curves. Hartley *et al.* pointed out that, if the law of mass action holds, it is not possible for a homogeneous liquid mixture to show a discontinuous change of density with composition at constant temperature and pressure, unless there is a sudden change in the equilibrium constant of one of the systems.

The published data for ethanolic solutions of pyridine showed considerable discrepancies, and marked discontinuities in the concentration–density curves were reported.

It thus seemed desirable to carry out a complete investigation of these systems. All measurements were made at 25° ± 0·005°, and the values of d quoted in the following tables are with reference to water at 4°.

Two types of pyknometer of volumes between 10 and 25 c.c. were used, one being the conventional Sprengel type (see Partington, "An Advanced Treatise on Physical Chemistry," Vol. II, 1951, Longmans), the other based on a suggestion by D. I. Stock (private communication). The latter was simple in design, consisting essentially of two parallel vertical capillary tubes of unequal length, their lower ends being connected by a

1 : 4-*Dioxan–water mixtures.*

$C_4H_8O_2$, % (w/w)	d	Mean	$C_4H_8O_2$, % (w/w)	d	Mean	$C_4H_8O_2$, % (w/w)	d	Mean
0	0·99706		50·37	1·03261		90·72	1·02943	
	0·99705	0·99706		1·03255	1·03258		1·02937	1·02940
11·21	1·00605		59·96	1·03602		95·28	1·02840	
	1·00599	1·00602		1·03613	1·03607		1·02848	1·02844
20·10	1·01360		66·42	1·03702		99·06	1·02820	
	1·01370	1·01365		1·03694	1·03698		1·02812	1·02816
30·07	1·02105		69·82	1·03703		100·00	1·02806	
	1·02101	1·02103		1·03696	1·03700		1·02810	1·02808
39·68	1·02704		80·02	1·03490				
	1·02695	1·02700		1·03494	1·03492			

Pyridine–water mixtures.

C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean
0	0·99707		35·58	1·00257		75·06	0·99967	
	0·99705	0·99706		1·00248	1·00253		0·99959	0·99963
5·07	0·99838		42·00	1·00281		82·03	0·99616	
	0·99833	0·99836		1·00280	1·00281		0·99605	0·99611
10·13	0·99937		50·21	1·00329		86·02	0·99307	
	0·99931	0·99938		1·00322	1·00326		0·99310	0·99309
19·86	1·00019		57·46	1·00311		89·38	0·98971	
	1·00014	1·00017		1·00303	1·00307		0·98979	0·98975
25·54	1·00166		59·38	1·00282		94·08	0·98467	
	1·00156	1·00161		1·00277	1·00280		0·98458	0·98463
30·05	1·00207		66·49	1·00208		100·00	0·97803	
	1·00201	1·00204		1·00216	1·00212		0·97797	0·97800

Pyridine–ethanol mixtures.

C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean	C_5H_5N, % (w/w)	d	Mean
0	0·78506		41·78	0·87214		80·07	0·94430	
	0·78510	0·78508		0·87205	0·87210		0·94422	0·94426
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29·67	0·84713		69·11	0·92907				
	0·84705	0·84709		0·92898	0·92903			

Acetone–water mixtures.

$COMe_2$, % (w/w)	d	Mean	$COMe_2$, % (w/w)	d	Mean	$COMe_2$, % (w/w)	d	Mean
0	0·99706		39·98	0·93726		80·74	0·84210	
	0·99705	0·99706		0·93722	0·93724		0·84219	0·84205
9·82	0·98571		51·43	0·91406		89·15	0·81875	
	0·98574	0·98573		0·91398	0·91402		0·81864	0·81872
21·23	0·96937		60·49	0·89369		100·0	0·78512	
	0·96941	0·96939		0·89364	0·89367		0·78502	0·78507
29·62	0·95616		71·89	0·86582				
	0·95605	0·95611		0·86574	0·86578			

cylindrical bulb. The upper ends of the tubes were fitted with ground-glass caps and were at the same horizontal height so that the bulb was at an angle to both limbs. It was found that, if the apparatus was filled in the inverted position through the shorter limb no troublesome " air-locks " occurred. Most of the observations were made in duplicate with the latter type of pyknometer.

Discussion.—The data for the dioxan solutions agree well with those of Hovorka *et al.* and extend the work below 35% of dioxan. The minimum at 1% of water reported by Geddes was not found.

The results for the pyridine–water mixtures lie on a smooth curve and agree well with those of Hartley, Thomas, and Applebey, the temperature difference being taken into account.

Ethanolic solutions of pyridine proved to be the most difficult to investigate, as both liquids are very hygroscopic. A blank series of estimations showed variations of 4 and 5 units in the fourth place of decimals after solutions had been exposed to the atmosphere for 10 minutes. The results indicate that the density varies continuously with concentration.

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$$d = 0{\cdot}99706 - 1{\cdot}091 \times 10^{-3}p_s - 9{\cdot}93 \times 10^{-6}p_s^2 - 3{\cdot}52 \times 10^{-9}p_s^3$$

The maximum difference between the experimental and calculated results was 0·0003.

Experimental

The organic solvent was distilled in all-glass apparatus directly into a roughly calibrated flask containing a known weight of conductivity water or alcohol under nitrogen. When the approximately correct volume had been collected the flask was re-weighed. The mixed solvent was transferred to the pyknometers either by blowing it over from the collecting flask through all-glass apparatus by means of dry nitrogen, or by " sucking " it over under reduced pressure.

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Commercial acetone was fractionally distilled and treated by Shipsey and Werner's method (*J.*, 1913, **103**, 1255) as modified by Livingston (*J. Amer. Chem. Soc.*, 1947, **69**, 1220). The product was refluxed with potassium permanganate, dried (K_2CO_3), and distilled in a stream of dry nitrogen; it had b. p. 56·20°/760 mm.

Pyridine (commercial) was distilled, and the 113—116° fraction repeatedly refluxed with potassium permanganate and sodium hydroxide until the solution retained its characteristic colour. The product was then fractionally distilled in a stream of dry nitrogen and dried over ignited barium oxide; it had b. p. 114·48°/760 mm.

Ethanol (99%) was treated by Donner and Hildebrand's method (*J. Amer. Chem. Soc.*, 1922, **44**, 2824) for the removal of aldehydes and heated under reflux over fresh lime. The product was boiled with anhydrous copper sulphate whilst a stream of nitrogen was passed through it, and finally redistilled over amalgamated aluminium chippings; it had b. p. 78·30°/760 mm.

All solvents were stored under nitrogen in sealed glass containers and redistilled in a stream of nitrogen immediately before use.

The water used in the mixtures was good-quality conductivity water.

Battersea Polytechnic, London, S.W.11. [*Received, November 20th*, 1951.]

242. *Preparation of Optically Active Lysine labelled with* ^{14}C *and* ^{15}N.

By H. R. V. Arnstein, G. D. Hunter, H. M. Muir, and A. Neuberger.

Syntheses of [*carboxy*-^{14}C], [α-^{14}C], and [α-^{15}N]lysine are described. The attempted separation of the [α-^{14}C]-labelled enantiomorphs by addition of optically active carrier lysine was not completely successful owing to extensive coprecipitation, which was demonstrated by an enzymic assay of the products. The L-[α-^{15}N]lysine was prepared in 90% yield from $^{15}NH_3$ by utilizing the inversion of configuration which occurs when the D-bromo-acid is treated with ammonia.

For metabolic studies to be reported elsewhere, we required L-lysine labelled with ^{14}C at the α- and the carboxyl-carbon atom severally and with ^{15}N as one of the two nitrogen atoms. Various syntheses of labelled lysine have been reported in the American literature. Thus, Weissman and Schoenheimer (*J. Biol. Chem.*, 1941, **140**, 779) utilizing the method of Eck and Marvel (*ibid.*, 1934, **106**, 387) obtained this amino-acid labelled with deuterium and ^{15}N in the α-position. DL-Lysine containing ^{15}N in the ε-position was prepared by condensation of labelled potassium phthalimide with ethyl 6-bromo-2-carbethoxy-2-phthalimidohexanoate * (Fink, Enns, Kimball, Silberstein, Bale, Madden, and Whipple, *J. Exp. Med.*, 1944, **80**, 455). Recently two groups of workers utilized the method of Fischer and Weigert (*Ber.*, 1902, **35**, 3772) for the preparation of lysine labelled with ^{14}C in the ε-position (Olynyk, Camp, Griffith, Woislowski, and Helmkamp, *J. Org. Chem.*, 1948, **13**, 465; Borsook, Deasy, Haagen-Smit, Keighley, and Lowy, *J. Biol. Chem.*, 1948, **176**, 1383).

In isotope work it is desirable to introduce the labelled atom at the latest possible stage of the synthesis. None of the methods described above was therefore thought suitable for our purpose and this also applies to various synthesis of lysine recently reported (Warner and Moe, *J. Amer. Chem. Soc.*, 1948, **70**, 3918; Degering and Boatright, *ibid.*, 1950, **72**, 5137; Gagnon and Boivin, *Canad. J. Res.*, 1948, **26**, *B*, 503). In the present work DL-[*carboxy*-^{14}C]lysine was obtained by an adaptation of Adamson's synthesis (*J.*, 1939, 1564). Methyl 2-keto*cyclo*hexane-1-[^{14}C]carboxylate was prepared by carboxylation of the sodium derivative of *cyclo*hexanone with [^{14}C]carbon dioxide, the procedure being a modification of that used by Levine and Hauser (*J. Amer. Chem. Soc.*, 1944, **66**, 1768). It was then treated with hydrazoic acid in chloroform in the presence of dry hydrogen chloride under the conditions used by Adamson (*loc. cit.*) for the corresponding ethyl ester. Hydrolysis with hydrochloric acid gave α-aminopimelic acid from which was obtained, under the usual conditions of the Schmidt reaction, lysine which was isolated as the dipicrate. This was converted into DL-lysine monohydrochloride on which all radioactive assays were carried out. The net yield of [*carboxy*-^{14}C]lysine was 12·2%, based upon the barium [^{14}C]carbonate used. An adaptation of Gaudry's synthesis (*Canad. J. Res.*, 1948, **26**, *B*, 387) to small-scale work for the synthesis of [*carboxy*-^{14}C]lysine has been reported by Borsook, Deasy, Haagen-Smit, Keighley, and Lowy (*J. Biol. Chem.*, 1950, **184**, 529): the yield stated was similar (10—15%), but the method is based on the more expensive sodium [^{14}C]cyanide.

DL-Lysine labelled with ^{14}C at the α-carbon atom was synthesized as follows: 4-Chlorobutan-1-ol, obtained from tetrahydrofuran (Starr and Hixon, *J. Amer. Chem. Soc.*, 1934, **56**, 1595), was converted into the chloro-bromide by an adaptation of the method of Cloke, Anderson, Lachmann, and Smith (*ibid.*, 1931, **53**, 2791). The chloro-bromide in slight excess was then caused to react with potassium phthalimide to give, apart from the desired *n*-chlorobutylphthalimide, some 1 : 4-diphthalimidobutane. The chloro-compound on treatment with sodium iodide in acetone yielded 4-iodobutylphthalimide. The latter was condensed with ethyl phthalimido[α-^{14}C]malonate, prepared from ethyl [α-^{14}C]malonate (*Org. Synth.*, 1927, **7**, 34, 78). The condensation product which was not isolated was heated under reflux with a mixture of hydrochloric and acetic acids. A somewhat similar

* Geneva nomenclature, $CO_2H = 1$.

synthesis of α-labelled DL-lysine using ethyl acetamidocyanoacetate has recently been described by Fields, Walz, and Rothchild (*J. Amer. Chem. Soc.*, 1951, **73**, 1000).

A dilution or carrier technique has been used with apparent success in the "resolution" of labelled cystine and methionine by Wood and Gutmann (*J. Biol. Chem.*, 1949, **179**, 535) and also in that of labelled glutamic acid by Kögl, Halberstadt, and Barendregt (*Rec. Trav. chim.*, 1949, **68**, 387). This method consists in adding an excess of unlabelled optically active amino-acid to the synthetic racemic labelled compound and then recrystallizing the optically active substance or a suitable derivative to constant radioactivity. In principle such a method should be particularly applicable to all cases in which the solubility of the optically active amino-acid or that of its chosen derivative is not markedly greater than that of the corresponding racemic compound. Preliminary experiments had shown that the solubilities of L-lysine picrate and DL-lysine picrate in water at 26° were approximately identical (about 0·65 g. per 100 c.c.). It was thus to be expected that, in absence of co-precipitation, addition of L-lysine in considerable excess to the labelled DL-lysine and crystallization of the picrate from a sufficiently large volume of solvent should yield a preparation of L-lysine substantially free from the labelled D-enantiomorph. An excess of carrier L-lysine (5 mmole) was therefore added to the solution of DL-[α-^{14}C]lysine (1 mmole) obtained from the hydrolysis of the phthalimido-compound. The mixture was then converted into the picrate which was crystallized from a volume of water calculated to be more than sufficient to retain the D-[α-^{14}C]lysine picrate together with a somewhat larger amount of L-lysine picrate of much lower specific radioactivity. D-[α-^{14}C]Lysine picrate was isolated from the mother-liquor in a similar manner after addition of a ten-fold excess of unlabelled D-lysine. The two optically active picrate fractions were recrystallized until the radioactivity remained essentially constant. The mother-liquors of all the above fractions were combined and the lysine picrate converted into the free amino-acid which was racemized by 20% hydrochloric acid at 170°.

This method of "resolution" rests on the assumption that the solubility of DL-lysine picrate in water is not affected by the presence of a large excess of the picrate of the optically active lysine. However, this may not be justified since it has been shown, with the aid of radioactive tracers, that extensive co-precipitation can take place between derivatives of different amino-acids (Keston, Udenfriend, and Cannan, *J. Amer. Chem. Soc.*, 1949, **71**, 249). Such a co-precipitation, if it occurred to a moderate extent, could not be readily demonstrated by measuring optical rotation, *e.g.*, the solution which is obtained on addition of 5 parts of unlabelled L-lysine to one part of labelled DL-lysine contains L- and D-lysine in the proportion of 11 : 1, whilst the total radioactivities of the two fractions are equal. The specific radioactivity of the D-lysine is therefore 11 times greater than that of the L-lysine. Contamination of the L-lysine picrate with 1% of D-lysine picrate, which would be difficult to demonstrate by classical methods or simple radioactivity measurements, would thus mean that about 10% of the radioactivity of the L-lysine fraction is due to D-lysine. It was therefore decided to examine the purity of these fractions by more specific techniques. Gale and Epps (*Biochem. J.*, 1944, **38**, 232) have shown that the purified cell-free preparation of lysine decarboxylase obtained from *Esch. coli* or *Bact. cadaveris* is stereochemically specific for L-lysine, and the reaction goes almost to completion and is not inhibited by the D-isomer. In separate experiments, radioactive L-lysine and radioactive D-lysine obtained from the picrates described above were therefore mixed with a known excess of unlabelled DL-lysine and incubated with a relatively large amount of enzyme; the cadaverine resulting from the L-lysine and also the unchanged D-lysine were isolated as the dibenzamido-derivatives (cf. Neuberger and Sanger, *Biochem. J.*, 1944, **38**, 125), and their radioactivities were determined and compared with that of the original lysine mixture. Results showed that about 10—12% of the radioactivity of the L-lysine fraction was due to D-lysine. This agrees with the observed decrease in the radioactivity of the L-lysine picrate during the first recrystallization. With the D-lysine fraction, for which conditions for "resolution" were somewhat less favourable, contamination (in terms of radioactivity) with the L-enantiomorph was about 20%. It is probable that more extensive recrystallization with large volumes of solvents might have eliminated the contaminating enantiomorphs. Such a procedure was, however, not practicable in view of the large losses of radioactive material

which it entails. It thus appears preferable to use methods of resolution not involving addition of carriers.

The method which was employed to introduce ^{15}N into the α-position of lysine yields without any resolution L-lysine which is almost optically pure. Reaction of an α-bromo-acid with ammonia is generally a nucleophilic bimolecular substitution and thus inversion of configuration occurs (Neuberger, *Adv. Protein Chem.*, 1948, **4**, 297; Brewster, Hughes, Ingold, and Rao, *Nature*, 1950, **166**, 178). ε-Benzoyl-D-lysine (Neuberger and Sanger, *loc. cit.*) was therefore converted with nitrosyl bromide into the optically active 6-benzamido-2-bromohexanoic acid, a reaction in which configuration is fully retained. The D-bromo-acid was then treated with 2·4 mols. of ^{15}N-labelled ammonia. The resulting ε-benzoyl-L-[α-^{15}N]lysine was hydrolysed to the free amino-acid which contained about 5% of the D-enantiomorph. Since the excess of $^{15}NH_3$ was fully recovered, the yield in terms of isotope was about 90%. This method of synthesizing amino-acids which contain ^{15}N and are optically almost pure can be extended to most other α-amino-acids.

Experimental

Radioactivity Determinations.—All radioactivity determinations were carried out on samples of " infinite thickness " (Popják, *Biochem. J.*, 1950, **46**, 560). Background of the instrument was 8—10 counts/min., and a sample containing 10^{-3} μc of ^{14}C per mg. of substance gave approx. 1100 counts/min. when counted as described. Sufficient counts to give a standard error of ±1—2% were taken, but slight variations in disc size introduced an additional error of ±3%.

^{15}N *Determinations.*—These were done with the mass spectrometer after combustion of the samples by the Kjeldahl procedure.

Preparation of Methyl 2-Ketocyclohexane-1-[^{14}C]*carboxylate.*—In a 100-c.c. three-necked round-bottomed flask with ground-glass joints equipped with a mercury-sealed stirrer, separating funnel, and reflux condenser was placed commercial anhydrous liquid ammonia (50 c.c.). To the stirred solution were added the minimum amount of sodium necessary to produce a blue colour, and a few small crystals of ferric nitrate, followed by 1·4 g. of sodium. When the sodium was all converted into sodamide, *cyclo*hexanone (5·0 g.) in absolute ether (30 c.c.) was added during 5 minutes. Ammonia was removed as rapidly as possible by warming and ether added to keep the volume to about 60 c.c. After the ether had been refluxing for a few minutes, the bath was removed, and the mercury-sealed stirrer replaced as rapidly as possible by a magnetic-induction stirrer. The reflux condenser and separating funnel were then removed and the flask was fitted on to a manifold of a high-vacuum system. After cooling of the ethereal suspension in liquid air, the vacuum system was evacuated to 0·001 mm., and then isolated from the vacuum pump.

The ethereal suspension was then allowed to warm to −15°, and carboxylation was carried out with stirring (Calvin, Heidelberger, Tolbert, Reid, and Yankwich, " Isotopic Carbon," Wiley, New York, 1949, p. 177) and use of [^{14}C]carbon dioxide liberated from barium [^{14}C]carbonate (11·0 g., 7·21 mc.). After 1 hour, excess of [^{14}C]carbon dioxide was removed and trapped in barium hydroxide solution.

After the reaction mixture had come to room temperature, the minimum amount of water was added to enable a satisfactory separation from the ethereal layer to be carried out. The aqueous phase was cooled to 0° in a three-necked flask fitted with a dropping funnel and gas inlet and outlet tubes. 50% Excess of ice-cold 20% sulphuric acid was added drop by drop, while a slow stream of nitrogen was passed through the flask. The [^{14}C]carbon dioxide evolved was trapped in a chain of absorbers containing N-sodium hydroxide and saturated aqueous barium hydroxide.

The liberated β-keto-acid was extracted into ether, and converted into methyl 2-keto*cyclo*hexane-1-[^{14}C]carboxylate as described by Levine and Hauser (*loc. cit.*). Distillation *in vacuo* yielded 3·0 g. of pure ester. 4·52 G. of barium [^{14}C]carbonate was recovered, containing a total activity of 1·80 mc.

DL-[α-carboxy-^{14}C]*Lysine.*—The conversion of the methyl 2-keto*cyclo*hexane-1-[^{14}C]carboxylate into DL-lysine dipicrate followed the experimental procedure outlined by Adamson (*loc. cit.*) for the corresponding ethyl ester. The crude dipicrate was converted into DL-lysine monohydrochloride which, after purification, had a total activity of 0·66 mc (12·2%) in 1·1 g. of the dihydrated salt.

4-Chlorobutylphthalimide.—4-Chloro-*n*-butyl bromide (75 g.) and potassium phthalimide, ground together, were heated under reflux for 6 hours and then cooled. Water (250 c.c.) was

added and the mixture shaken until the solid was granular. The precipitate was filtered off, washed with water, and dried. The material was then dissolved in hot ethanol (500 c.c.) and filtered hot. On concentration to 250 c.c. a further precipitate was obtained. The *monophthalimide* crystallized on further concentration and cooling to 0°. It was recrystallized from a small amount of ethanol and had m. p. 76·5° (yield, 50% in terms of potassium phthalimide) (Found: C, 59·7; H, 5·1; N, 5·9; Cl, 14·9. $C_{12}H_{12}O_2NCl$ requires C, 60·6; H, 5·1; N, 5·9; Cl, 14·9%). The materials which were relatively insoluble in warm ethanol were combined, washed again with ethanol, and, after drying, recrystallized from glacial acetic acid. 1 : 4-Diphthalimidobutane, recrystallized again from a large amount of ethanol, had m. p. 224° (Found: C, 69·1; H, 4·5; N, 7·9. Calc. for $C_{20}H_{16}O_4N_2$: C, 69·4; H, 4·6; N, 8·0%). Langenbeck, Woltersdorf, and Blachnitzki (*Ber.*, 1939, **72**, 671) give m. p. 219°.

4-*Iodobutylphthalimide*.—A solution of the above chloro-compound (35·5 g.) in acetone (400 c.c.) containing sodium iodide (37 g.) was boiled for 6 hours. Removal of sodium chloride and evaporation to dryness gave the crude iodo-compound which was recrystallized from ethanol and then had m. p. 88—89°. Gabriel (*Ber.*, 1909, **42**, 1249) gives m. p. 88—89·5°.

Ethyl Phthalimido[α-^{14}C]*malonate*.—To a solution of ethyl [α-^{14}C]malonate (0·206 g.; 1·44 mc; obtained from the Radiochemical Centre, Amersham) in dry, freshly distilled carbon tetrachloride (20 ml.) was added a small excess of bromine (0·212 g). in carbon tetrachloride (3·6 c.c.). After 1 hour, when the bromination appeared to be complete, carrier bromomalonate (1·31 g.) was added. The solution was kept at room temperature for 16 hours. The solvent was then removed in a stream of dry air at room temperature. The residue was dissolved in dry toluene (20 ml.) and heated with potassium phthalimide (1·146 g., 10% excess) in a sealed tube at 120—130° for 2 hours and then at 140° for 2 hours. The solution was filtered and the residue extracted with benzene. The solid (1·1 g., 7·0 μc) was discarded and the filtrate evaporated to dryness in a stream of dry air. After addition of carrier ethyl phthalimidomalonate (1·06 g.) the product was recrystallized from ether–light petroleum (b. p. 60—80°), yielding ethyl phthalimido-[α-^{14}C]malonate (2·35 g.).

DL-[α-^{14}C]*Lysine*.—Ethyl phthalimido[^{14}C]malonate (2·087 g., 6·85 mmoles) in dry ethanol (15 ml.) was cooled quickly by immersion in liquid air and simultaneously a solution of sodium (0·186 g.) in dry ethanol was added. The solvent was removed *in vacuo*, giving ethyl sodiophthalimido[α-^{14}C]malonate. 4-Iodobutylphthalimide (2·57 g.) was added and the mixture heated at 150—155° for 3 hours. After addition of dry toluene (5 c.c.) heating was continued for further 20 minutes. The toluene was then removed and the residue refluxed for 20 hours with a mixture of concentrated hydrochloric acid (30 c.c.) and acetic acid (15 c.c.) and then evaporated to dryness *in vacuo*; water (40 c.c.) was added and the mixture continuously extracted with ether for 48 hours. The ethereal extract, which was only feebly radioactive, was discarded. The aqueous layer was concentrated to dryness *in vacuo*, giving crude DL-[α-^{14}C]lysine dihydrochloride. The product was dissolved in water, and the solution filtered and used directly for the following operations.

Isolation of L-[α-^{14}C]*Lysine Picrate*.—The L-lysine which was used as carrier had been obtained by hydrolysis of casein with hydrochloric acid. It had $[\alpha]_D^{22}$ +24·9° (*c*, 5·0 in 5N-hydrochloric acid). The recorded values vary somewhat; thus Dunn and Rockland (*Adv. Protein Chem.*, 1947, **3**, 354) quote the unpublished value of $[\alpha]_D^{25}$ +25·72° (*c*, 1·64 in 6·08N-hydrochloric acid), but Greenstein, Gilbert, and Fodor (*J. Biol. Chem.*, 1950, **182**, 451) give $[\alpha]_D$ +23·0°. All values for specific rotation are stated in terms of the free amino-acid. It is unlikely that our L-lysine carrier contained more than 2—3% of the D-enantiomorph. The carrier L-lysine dihydrochloride (7·74 g., 35 mmoles) was added to the above solution of DL-[α-^{14}C]lysine. After adjustment of the pH to 6·0 with 1·94N-sodium hydroxide (27·5 c.c.), picric acid (9·58 g., 41·85 mmoles) and 1·94N-sodium hydroxide (21·6 c.c., 41·85 mmoles) were added. Water was added to a final volume of 400 c.c. and the mixture heated until clear. After 24 hours at 0° the L-lysine picrate (10 g., 127 μc) was filtered off. Recrystallization from water (200 c.c.) afforded 9·0 g. of material having a specific radioactivity of 9·76 μc/g. After two further recrystallizations an apparently constant value was obtained; thus with successive recrystallizations of a small portion the specific radioactivities were 9·33, 9·00, 8·97 μc/g. respectively.

Isolation of D-[α-^{14}C]*Lysine Picrate*.—To the mother-liquors from the above isolation of L-[α-^{14}C]lysine picrate, D-lysine monohydrochloride {6·4 g., 35 mmoles; $[\alpha]_D^{22}$ −24·1° (*c*, 2·5 in 6N-hydrochloric acid)}, 1·94N-sodium hydroxide (18·0 c.c., 35 mmoles), and picric acid (8·02 g., 35 mmoles) were added; the picrate crystallized from the solution (800 c.c.). There were obtained 9·8 g. of material with specific radioactivity of 9·27 μc/g. Recrystallization of a portion

(0·709 g.) from water (25 c.c.) afforded a sample with essentially unchanged radioactivity (9·33 μc/g.).

Isolation of D- *and* L-[α-^{14}C]*Lysine from the Picrates.*—To a solution of L-[α-^{14}C]lysine picrate (9·0 g.) in hot water (100 c.c.) was added concentrated hydrochloric acid (5 c.c.), and the solution continuously extracted with hot benzene until the aqueous layer was no longer yellow. The aqueous solution was then evaporated to dryness *in vacuo* and the residue crystallized from aqueous ethanol by addition of pyridine. Recrystallization from aqueous ethanol afforded L-[α-^{14}C]lysine monohydrochloride monohydrate (3·531 g.; specific radioactivity 15·3 μc/g.). From the mother-liquors a further crop (0·55 g.) was obtained. The total yield of L-[α-^{14}C]lysine was 62·5 μc. D-[α-^{14}C]Lysine picrate was similarly converted into the monohydrochloride monohydrate (4·348 g., specific radioactivity 16·5 μc/g.). The mother-liquor yielded a further 0·35 g., the total yield being 77·6 μc.

Isolation of DL-[α-^{14}C]*Lysine.*—The picrate from the combined mother-liquors was converted into lysine and racemization completed by heating this in 20% hydrochloric acid (60 c.c.) at 170° for 18 hours. The DL-lysine was precipitated as phosphotungstate which was converted into the monohydrochloride monohydrate (3·2 g.). Purification *via* the benzylidene copper complex (Turba, *Z. physiol. Chem.*, 1948, **283**, 19; 3·3 g.; 57 μc) yielded DL-[α-^{14}C]lysine dihydrochloride (2·56 g.; 52·5 μc). The specific radioactivities of the three fractions of radioactive lysine are given in the following Table which also shows the calculated radioactivities based on those of the barium carbonate obtained by wet combustion (Van Slyke and Folch, *J. Biol. Chem.*, 1940, **136**, 509) of the lysine hydrochlorides.

Specific radioactivities of [α-^{14}C]*lysine fractions.*

Compound	Radioactivity (μc/mmole)	Compound	Radioactivity (μc/mmole)
L-Lysine monohydrochloride monohydrate :		DL-Lysine dihydrochloride :	
(*a*) directly	3·1	(*a*) directly	4·5
(*b*) calc. from $BaCO_3$	3·1	(*b*) calc. from $BaCO_3$	4·4
(*c*) from picrate	3·2	(*c*) from benzylidene Cu complex	4·6
D-Lysine monohydrochloride monohydrate :		(*d*) from recryst. picrate	4·8
(*a*) directly	3·3		
(*b*) calc. from $BaCO_3$	3·4		
(*c*) from picrate	3·3		

Although the relatively high specific radioactivity of the racemic lysine compared with the two optically active fractions is not easy to explain, this discrepancy is probably not due to an impurity, as the radioactivity measurements of the various derivatives are in good agreement. The total radioactivity in all three fractions was 192 μc, corresponding to a yield of 18·9% based on ethyl[α-^{14}C]malonate.

Enzyme Experiments.—The crude decarboxylase was obtained as described by Gale and Epps (*loc. cit.*). The organism *Bact. cadaveris* (National Collection of Type Cultures, no. 6578) was grown by Dr. M. R. Pollock, to whom we express our gratitude. The cells, after incubation, were thoroughly washed and the suspension was poured into acetone (5 vols.) cooled to −10°. On repeated washing with cold acetone, centrifugation, and drying, a powder was obtained which gave Q_{CO_2} values for L-lysine at 30° and pH 6 of approx. 250. In several experiments the enzyme was further purified as described by Gale and Epps.

A warm solution of L-[α-^{14}C]lysine picrate (78·9 mg.; specific radioactivity, 9·4 × 10^{-3} μc/mg.) and DL-lysine hydrochloride monohydrate (0·5005 g.) in concentrated hydrochloric acid (10 c.c.) was extracted continuously with warm benzene until colourless. It was then concentrated to dryness, and the residue taken up in water and again concentrated to dryness *in vacuo*. The dihydrochloride was dissolved in water, and the solution brought to pH 6·0 by addition of N-sodium hydroxide and made up to 35 ml. Enzymic decarboxylation was carried out by incubation at 30° for 2 hours of a mixture containing 15 ml. of phosphate buffer (pH 6·0), 15 ml. of the lysine solution, and usually about 7·0 ml. of the enzyme solution. The amount of enzyme chosen was three times that required to decarboxylate the L-lysine present in 20 minutes under the conditions used. The activity of the enzyme preparation was estimated manometrically immediately before the experiment. At the end of the incubation the protein was coagulated by heat; the solution was filtered and made alkaline. Benzoylation (benzoyl chloride, 0·72 g.; N-sodium hydroxide, 6·5 c.c.) gave dibenzoylcadaverine which, recrystallized several times from small volumes of ethanol, had m. p. 134—135° (von Braun, *Ber.*, 1904, **37**, 3583, gives m. p.

135°). The dibenzoyl-D-lysine could not be obtained crystalline in the experiment. The specific radioactivity of the dibenzoylcadaverine was 800×10^{-6} μc/mg.; the value calculated from that of the picrate and the amount of non-radioactive DL-lysine added on the assumption that all radioactive lysine in the mixture had the L-configuration was 920×10^{-6} μc/mg. The difference between the observed and the calculated radioactivity indicates that about 15% of the radioactivity in the original lysine used was due to the D-enantiomorph. Another enzyme experiment gave a similar value of 12·8%.

The optical purity of the D-[α-^{14}C]lysine picrate was also investigated by the decarboxylase method. In this experiment the dibenzoyl-D-lysine was obtained crystalline by acidification of the mother-liquor left from the crystallization of the dibenzoylcadaverine; recrystallized several times from acetone it had m. p. 145—146° (Neuberger and Sanger, *loc. cit.*, give m. p. 145°). The specific radioactivity of the dibenzoylcadaverine was 310×10^{-6} μc/mg. whilst that of the dibenzoyl-D-lysine was 1220×10^{-6} μc/mg. This and a parallel experiment indicated that the D-lysine preparation contained 19—23% of the L-enantiomorph in terms of radioactivity.

ε-*Benzoyl*-L-[α-^{15}N]*lysine*.—D-6-Benzamido-2-bromohexanoic acid (7·3 g.), from D-lysine (Neuberger and Sanger, *loc. cit.*), was added to a solution of [^{15}N]ammonia (62·5% isotope excess) containing 0·95 g. (2·4 equivs.) of $^{15}NH_3$. The container was tightly corked and kept for 4 days at 40°. The solution was then acidified to pH 6·0 with hydrochloric acid, and the solid (4·24 g.) collected and dried (73%) The material was recrystallized by dissolution in acid and addition of sodium acetate. The excess of [^{15}N]ammonia was recovered by addition of alkali to the original mother-liquor and distillation into dilute sulphuric acid.

L-[α-^{15}N]*Lysine Dihydrochloride*.—The ε-benzoyl compound (3·0 g.) was heated under reflux with concentrated hydrochloric acid for 20 hours. Excess of acid was removed by two evaporations to dryness. The residue was dissolved in water and brought to pH 5. Sodium hydroxide (1 equiv.) and picric acid (3·0 g.) were then added. The mixture was heated until clear. The crystalline picrate obtained on cooling to 0° was recrystallized from water and decomposed as described above; the lysine crystallized first as monohydrochloride monohydrate and then as dihydrochloride, $[\alpha]_D^{20}$ (in terms of lysine) +22·4° (*c*, 4·00 in 5% hydrochloric acid). Isotope analysis showed 31·1% excess ^{15}N.

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243. *The Action of γ-Radiation on Aqueous Solutions of Cysteine.*

By A. J. SWALLOW.

It is shown that dilute aqueous solutions of cysteine hydrochloride are oxidised by the action of γ-radiation, and that for air-saturated solutions the ionic yield increases with concentration. For a 0·051M-solution of cysteine hydrochloride the ionic yield is 24, which is too great to be explained without postulating a chain reaction. In the absence of dissolved oxygen the ionic yield for a 0·051M-solution is 3. These results are explained by equations which may have implications for enzyme chemistry.

THE deactivation of enzymes in solution by ionizing radiations can be inhibited by the addition of various protective substances (Dale, *Biochem. J.*, 1942, **36**, 80; *Brit. J. Radiol.*, 1947, Suppl. No. 1, 46). It is generally considered that these substances act by competing with active groups of the enzyme for the radicals produced by irradiation. Amongst other substances, those containing thiol groups have been used in studying the radiation chemistry of enzymes. For example, glutathione is a protective substance for ribonuclease (Collinson, Dainton, and Holmes, *Nature*, 1950, **165**, 266). The role of thiol groups in the enzymes themselves has been investigated by Barron, Dickman, Muntz, and Singer (*J. Gen. Physiol.*, 1948—49, **32**, 537; Barron and Dickman, *ibid.*, p. 595). The interesting result that cysteine caused *increased* deactivation of catalase while cystine protected it has been reported by Forssberg (*Nature*, 1947, **159**, 308). In the biological field, cysteine was one of the first

substances to be injected into rats or mice to protect them from the lethal effect of *X*-radiation (Patt, Tyree, Straube, and Smith, *Science*, 1949, **110**, 213).

It was thought of interest to study the effect of radiation on cysteine itself, partly with regard to its action as a protective substance, but more particularly for its own radiation chemistry. Recent work by Dale and Davies (*Biochem. J.*, 1951, **48**, 129) has been concerned with the production of hydrogen sulphide from cysteine, and Rotheram, Todd, and Whitcher (AECD, UCLA-119, 1951) have studied the oxidation of the thiol group and the formation of hydrogen peroxide and hydrogen sulphide in aqueous solutions of cysteine. Dale and Davies (*loc. cit.*) have also shown that deamination, which is important with other amino-acids, does not proceed appreciably with cysteine.

FIG. 1. *Irradiation of* 0·00051M-*cysteine* (*air-saturated*).

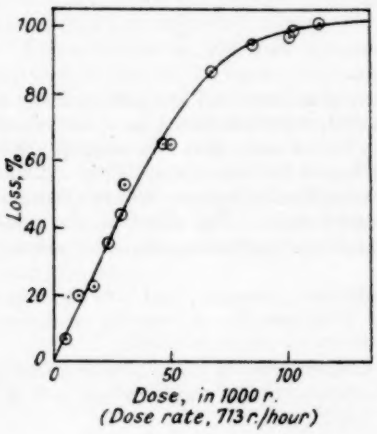


FIG. 2. *Irradiation of* 0·0051M-*cysteine* (*air-saturated*).

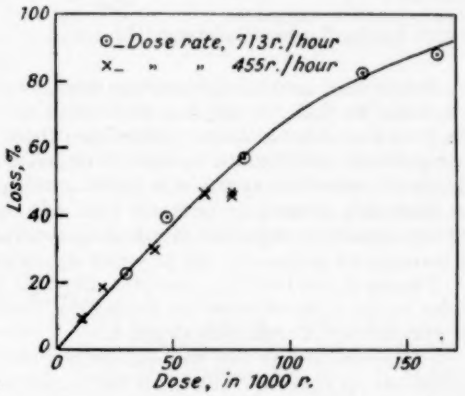
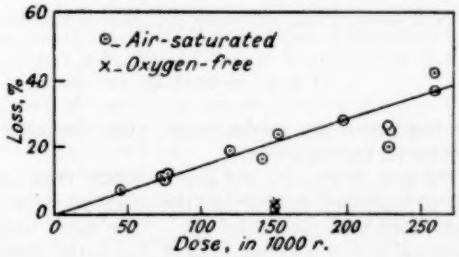


FIG. 3. *Irradiation of* 0·051M *cysteine* (*dose rate*, 455 r./hour).



It was decided to measure the decrease of cysteine concentration with irradiation, rather than to measure the amount of product formed. This method was adopted because one of the main products of irradiation was expected to be cystine, and this cannot be measured accurately in the presence of large amounts of cysteine.

Fig. 1 shows the results obtained for a 0·00051M-solution of cysteine hydrochloride, Fig. 2 those for 0·0051M, and Fig. 3 for 0·051M. All three curves are for air-saturated solutions. Stein and Weiss have found that after a certain dose the rate of reaction sometimes drops owing to the exhaustion of oxygen originally present in the solution (*J.*, 1949, 3245; Loebl, Stein, and Weiss, *J.*, 1950, 2704). This was not the case in these experiments because the rate of irradiation was so slow (455—713 r./hour), and the volume of solution so small, that air was able to dissolve continuously and keep the solutions nearly saturated.

During the irradiation of all these solutions the smell of hydrogen sulphide became noticeable, and colourless hexagonal crystals, presumably of cystine, separated from the two more concentrated solutions.

In the absence of dissolved oxygen the loss of cysteine from the 0·051M-solution was much less pronounced, and after a dose of 150 000 r. the cysteine concentration was still more than 0·049M. Results for oxygen-free cysteine are also shown on Fig. 3.

Experiments were conducted on the effect of γ-radiation on cystine. 0·025M-Solutions of cystine in 0·12M-hydrochloric acid were freed from oxygen and saturated with hydrogen. A dose of 52 300 r. produced 0·0003M-cysteine.

The ionic yields for all these reactions are presented in the following table.

0·00051M-Cysteine, air saturated	$2{\cdot}5 \pm 0{\cdot}3$	Molecules of cysteine lost (formed) per 32·5 ev absorbed
0·0051M- ,, ,,	$13 \pm 1{\cdot}5$	,, ,, ,, ,,
0·051M- ,, ,,	24 ± 3	,, ,, ,, ,,
0·051M-Cysteine, oxygen-free	$3 \pm 1{\cdot}5$	,, ,, ,, ,,
0·025M-Cystine, hydrogen saturated	2 ± 1	,, ,, ,, ,,

It has been usual to assume that the energy required to create an ion-pair in water is the same as that for air, *viz.*, 32·5 ev in the case of γ-radiation (see Lea, "Actions of Radiation on Living Cells," Cambridge, 1946). It is now known that this assumption is not justified and that the value 32·5 ev has no significance for aqueous systems. It was decided however to express ionic yields in this paper as molecules lost per 32·5 ev absorbed so that comparison may be made with other published results. The choice of the value 32·5 ev should be regarded as purely conventional, and the conclusions presented are not dependent on its having any physical significance.

The ionic yield of 24 is exceptionally high for radiation chemistry, and is of the same order as the yield reported by Rotheram, Todd, and Whitcher (*loc. cit.*) for the oxidation of cysteine by *X*-radiation at pH 8.

Discussion.—It is now well established that the primary step in the action of ionising radiations on aqueous solutions is the formation of hydrogen atoms and hydroxyl radicals (Weiss, *Nature*, 1944, **153**, 748; Stein and Weiss, *J.*, 1949, 3245):

$$H_2O \rightsquigarrow H + OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

In the presence of dissolved oxygen the following reaction is also to be expected to occur to a considerable extent:

$$H + O_2 \longrightarrow HO_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

so that strong oxidising conditions are predominant, even though both OH radicals and H atoms are initially produced by radiation.

The ionic yields for the loss of cysteine are much greater than could be accounted for solely by the production of hydrogen sulphide in the yields reported by Dale and Davies, and by Rotherham, Todd, and Whitcher (*locc. cit.*). The most readily formed oxidation product of cysteine is cystine, and it is assumed that that is the main product of the reactions studied here. Rotheram, Todd, and Whitcher also consider that cystine is the main product of irradiation.

The ionic yield of 24 for a 0·051M-solution is exceptionally high. It is difficult to explain it by any simple reaction of the radicals formed by the primary act, because even in water vapour the maximum possible number of radicals is 6 hydrogen and 6 hydroxyl from each 32·5 ev of energy absorbed (Dainton, *Ann. Reports*, 1948, **45**, 5). In liquid water the number is likely to be less (*idem*, *J. Phys. Coll. Chem.*, 1948, **52**, 490). A much more likely explanation is that a chain reaction is taking place. The system is very complex but the following equations are put forward tentatively to show how a chain reaction might take place:

$$RSH + OH \longrightarrow RS + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$RS + RSH \longrightarrow RS{\cdot}SR + H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where RSH is cysteine and RS·SR cystine. A reaction like that of equation (4) has been suggested previously for the photolysis of ethanethiol (Meissner and Thompson, *Trans. Faraday Soc.*, 1938, **34**, 1238). The hydrogen atom reacts with oxygen according to equation (2), and the HO_2 radical so formed reacts with cysteine :

$$HO_2 + R{\cdot}SH \longrightarrow R{\cdot}S{\cdot} + H_2O_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The hydrogen peroxide so formed may also react slowly with cysteine to increase the ionic yield, while the R·S· radical reacts according to equation (4).

Equations (4), (2), and (5) constitute a chain reaction. The chain can be terminated by many reactions, amongst which are the combination of H, OH, HO_2, and RS radicals. In the absence of oxygen, of course, the chain reaction would not proceed, and this explains the low ionic yield in the absence of dissolved air. In the more dilute solutions, the ionic yield is less, since the termination reactions compete more favourably with the reactions whose equations are given above.

The reduction of cystine to cysteine in the presence of hydrogen is not a chain reaction, and may be due to the reverse of reaction (4).

The existence of free thiol radicals has often been postulated and may be responsible for the action of certain enzymes (Waters, "Chemistry of Free Radicals," 2nd edn., Oxford, 1948, 73, 188, 257, 282). In fact, the reactions described above have many implications for enzyme chemistry, and it is hoped elsewhere to discuss the possibility that by radiation-chemical methods one may imitate more or less exactly the action of certain enzymes. The work of Weiss and his collaborators has provided valuable evidence in this field by showing that the products of biological reactions and of radiation-induced reactions are often the same.

Experimental

Cysteine.—The DL-cysteine hydrochloride used in these experiments was obtained from two sources, L. Light and Co. Ltd. and British Drug Houses Ltd. Results obtained with the two kinds were identical. Cysteine hydrochloride was always dried before use, as it is slightly deliquescent. Cysteine solutions were always fairly stable, and even for the longest irradiations with the most dilute solutions the decrease in cysteine concentration of a control due to normal air oxidation was not more than 12%. Freshly made solutions were always used for irradiations of 0·00051M- and 0·0051M-cysteine. For 0·051M-cysteine this was not necessary.

L-Cystine was obtained from British Drug Houses Ltd.

Water.—Water was specially purified by distillation from alkaline permanganate followed by redistillation and a second redistillation directly into the flask in which the solution was to be made. Pyrex apparatus was used throughout.

De-aeration.—The apparatus used for de-aeration is shown in Fig. 4. The tubes at the lower end of each limb were removed, and 1 ml. of purified water was introduced into each, followed by 1 ml. of the solution to be irradiated. The tubes were then replaced on the ground-glass joints which had been greased round the top with Apiezon L grease. Air was removed by alternate evacuation through a liquid-air trap and saturation with oxygen-free nitrogen (British Oxygen Company Ltd., Wembley) until the volume of the solutions was reduced to 1 ml. by evaporation. The whole apparatus was shaken to avoid bumping. The evacuation–saturation cycle had to be repeated about 12 times. Finally, the tap *A* was closed while the solutions were under a pressure of nitrogen a few cm. above atmospheric, and the lower part of the apparatus was detached at *B*.

A similar procedure, but with use of oxygen-free hydrogen, was adopted when preparing cystine for irradiation.

pH *of Solutions.*—No attempt was made to adjust all solutions of cysteine to the same pH or chloride concentration. The pH of 0·00051M-cysteine is 3·3, of 0·0051M, 2·6, and of 0·051M, 1·9. After irradiation with a dose of 100 000 r., the pH of the 0·00051M-solution had been reduced to 3·15. The decrease of pH did not cease when all the cysteine had been oxidised, presumably owing to the formation from cystine of further products such as cysteic acid.

Irradiation Arrangements.—0·00051M-Solutions and some 0·0051M-solutions were irradiated in the apparatus shown in Fig. 5. A 100-mc metallic source of ^{60}Co (from A.E.R.E., Harwell) was lowered into the central tube with a bar magnet. Other solutions were irradiated in flat-bottomed tubes, 1 cm. in diameter, fixed with elastic bands round a central tube con-

taining the ^{60}Co. Air-free and hydrogen-saturated solutions were arranged round the ^{60}Co in this way, and 2" lead blocks placed between the two limbs of the apparatus to protect the control solution from radiation. All solutions were irradiated at room temperature (5—15°) and no attempt was made to control this since it was not expected that the results would be sharply temperature-dependent. It may be, however, that some of the errors in the experiments are due to fluctuation in temperature.

Determination of Cysteine.—The method used was that of Kuhn, Birkofer, and Quackenbush (*Ber.*, 1939, **72**, 407), based on the reaction of cysteine with excess of iodine in glacial acetic acid. The exact procedure depended on the concentration of cysteine. The following was used for cysteine $\leqslant$ 0·00051M.

Cysteine solution (1 ml.) in a weighing bottle was evaporated to dryness on a steam-bath, and, when cool, water (two drops) was added, followed by distilled " AnalaR " glacial acetic

FIG. 4. *Apparatus for removing oxygen from solutions.*

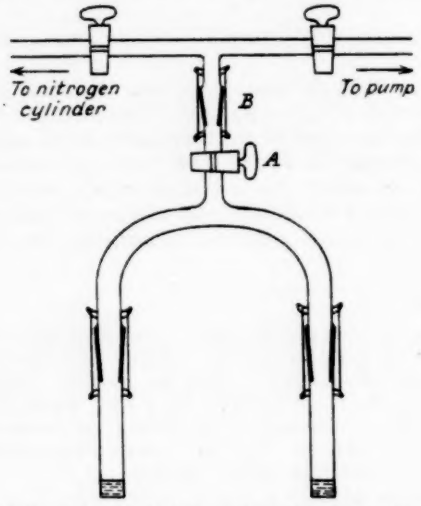
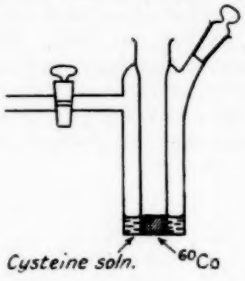


FIG. 5. *Irradiation apparatus.*



acid (1 ml.). A glacial acetic acid solution (0·5 ml.) of iodine was then added rapidly, followed after 1 minute by water (about 1·5 ml.). This solution was then titrated with 0·001N-sodium thiosulphate, starch being used as indicator. Since the reaction of cysteine with iodine did not proceed stoicheiometrically, it was necessary to calibrate with a freshly made standard solution of cysteine for each set of titrations. Typical results are shown in the following table.

Results of irradiating 0·00051M-*cysteine hydrochloride.*

Solution titrated	0·001N-$Na_2S_2O_3$ required, ml.	Concn. (M) of solution titrated	Decrease of concn. (M) during irradiation
0·00051M-Cysteine standard ...	0·18, 0·20, 0·20, 0·19, 0·20 Average = 0·194	0·00051	—
Irradiated solution (101 000 r.)	0·575, 0·56, 0·57, 0·59, 0·58 Average = 0·575	0·000025	0·000485
Control solution	0·245, 0·235, 0·23, 0·24, 0·24, 0·25 Average = 0·24	0·00045	0·00006
Blank (no cysteine)	0·57, 0·60, 0·605, 0·60, 0·57, 0·59, 0·605 Average = 0·595	0	—

The titration of 0·00051—0·0051M-cysteine was carried out in a similar manner except that only 0·1 ml. of cysteine was used.

In order to titrate 0·0051—0·051M-cysteine, 1 ml. of the solution was diluted to 10 ml., and 0·1-ml. quantities were used. No calibration was necessary in this case as the control solution could within the experimental limits be assumed to be exactly 0·051M.

The process of evaporation to dryness, mentioned above, was necessary to remove hydrogen sulphide. Solutions evaporated at room temperature in a vacuum desiccator gave the same result, but this procedure was slower.

The following substances were shown not to interfere with the determination: hydrogen sulphide, hydrogen peroxide, pyruvic acid, and glyceraldehyde.

Dose Measurement.—Dose measurement was by Day and Stein's chemical method (*Nucleonics*, 1951, **8**, No. 2, **34**). Aqueous solutions of benzene were irradiated to produce phenol, which was measured colorimetrically. The dose rate produced in the apparatus shown in Fig. 5 was 713 r./hour, and in the flat-bottomed tubes 455 r./hour.

This work was carried out while the author was first a Nuffield Research Fellow, and later an I.C.I. Fellow of the University of Birmingham.

DEPARTMENT OF PHYSICS, THE UNIVERSITY, BIRMINGHAM. [*Received, July 31st*, 1951.]

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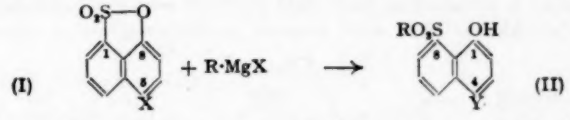
244. *Action of Grignard Reagents. Part IV.* Action of Grignard Reagents on Substituted Derivatives of Naphthasultone, N-Phenyl-o-sulphobenzoic Imide, 2-Phenyl-4 : 5-benzo-1 : 2-thiazolone, and 3-Chloro-4 : 5-benzo-1 : 2-thiazole 1 : 1-Dioxide.*

By AHMED MUSTAFA and MUSTAFA KAMAL HILMY.

The reactions named in the title occur as expected.

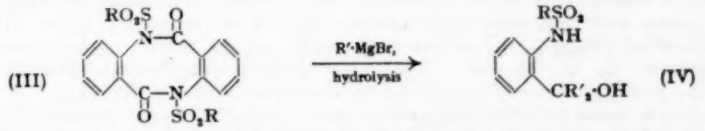
IN Parts I and III (Mustafa and Gad, *J.*, 1949, 384; Mustafa, *J.*, 1949, 2151), it was shown that the action of Grignard solutions on tolylene-3 : 4-sulphonylide and 1 : 8-naphthasultone (I; X = H), or its substitution products, provides a new method of preparing *o*- or *peri*-hydroxydiaryl sulphones respectively. Further examples are now reported.



When X in (I) is acetyl, the sultone ring is opened by reaction with methyl-, ethyl-, phenyl-, or α-naphthyl-magnesium halide, and (II) is obtained in which Y is CR_2·OH produced by reaction of the acetyl group with the Grignard reagent. 5-Benzoylnaphthasultone (I; X = $CO{\cdot}C_6H_5$) reacts similarly.

5-Chloromethyl-1 : 8-naphthasultone reacts with an excess of phenyl- or α-naphthylmagnesium bromide to give 4-benzyl-8-benzenesulphonyl- and 4-α-naphthylmethyl-8-α-naphthalenesulphonyl-1-naphthol, respectively (cf. Table 1*a*).

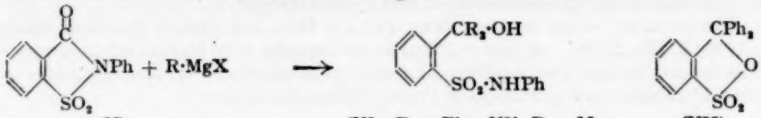
The constitutions of the products are deduced from the facts that they are colourless, form the corresponding methyl ethers with ethereal diazomethane in the absence of methyl alcohol (cf. Schönberg and Mustafa, *J.*, 1948, 605), dissolve in aqueous alkali, and contain active hydrogen.



Mustafa and Gad (*loc. cit.*) have shown that Grignard reagents break the –C–N– linkage of *NN'*-diarylsulphonyldianthranilides (III), giving the corresponding *o*-arylsulphonamidotriarylcarbinols (IV). *N*-Phenyl-*o*-sulphobenzoic imide (V) undergoes similar C–N cleavage, yielding the *N*-substituted *o*-sulphamyl-carbinols (VI*a*, *b*, and *c*) (cf. Sachs, Wolff, and Ludwig, *Ber.*, 1904, **37**, 3252; Sachs and Ludwig, *ibid.*, p. 389). The structure of *N*-phenyl-*o*-sulphamyltriphenylcarbinol (VI*a*) is inferred from the facts that it is colour-

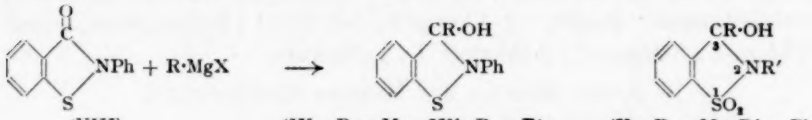
* Part III, *J.*, 1949, 2151.

less, reacts with ethereal diazomethane (cf. Mustafa and Gad, *loc. cit.*), contains active hydrogen, gives the expected molecular weight, and is not identical with (X) (see below). Those of (VI*b* and *c*) are similarly deduced. When (VI*a*) is treated with concentrated sulphuric acid, the sultone (VII) is obtained, together with aniline.



(V) (VI*a*, R = Ph; VI*b*, R = Me; VI*c*, R = Et) (VII)

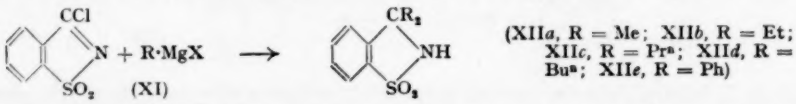
The carbonyl group of 2-phenyl-4 : 5-benzo-1 : 2-thiazolone (VIII) adds the Grignard reagent in the usual manner to give the corresponding hydroxy-compounds (IX*a*, *b*, and *c*)—compare the formation of (X*c*) by the action of phenylmagnesium bromide on saccharin (Oddo and Mingola, *Gazzetta*, 1927, **57**, 465), in contrast with the behaviour of (V) towards Grignard solutions. The constitution of the products (IX*a*—*c*) is elucidated from the facts



(VIII) (IX*a*, R = Me; IX*b*, R = Et; IX*c*, R = Ph) (X*a*, R = Me, R′ = Ph; X*b*, R = R′ = Ph; X*c*, R = Ph, R′ = H)

that they are colourless, contain active hydrogen, and are recovered unchanged when treated with ethereal diazomethane. When (IX*a*) and (IX*c*) are treated with hydrogen peroxide in acetic acid at 100°, they yield the 1 : 1-dioxides (X*a* and *b*).

The sultam (XII*e*) is obtained in poor yield together with the analogous sultim by the condensation of the chloride (XI) with benzene in the presence of aluminium chloride



(XI) (XII*a*, R = Me; XII*b*, R = Et; XII*c*, R = Pr^n; XII*d*, R = Bu^n; XII*e*, R = Ph)

(Fritzsche, *Ber.*, 1896, **29**, 2296). When (XI) has been treated with excess of phenylmagnesium bromide, hydrolysis gives (XII*e*) in almost quantitative yield. Methyl-, ethyl-, *n*-propyl-, and *n*-butyl-magnesium halides react analogously. This constitutes a new method for preparing these sultams.

Experimental

Action of Grignard Reagents on Substituted Naphthasultones (I).—The following exemplifies the procedure. 5-Acetyl-1 : 8-naphthasultone (I; X = Ac) (Schetty, *Helv. Chim. Acta*, 1947, **30**, 1650) (2 g.) in dry benzene (50 c.c.) was added to a solution of phenylmagnesium bromide [prepared from magnesium (1·8 g.), bromobenzene (18 g.), and dry ether (40 c.c.)], and the mixture was heated under reflux for 3 hours and then set aside overnight. The reaction mixture was decomposed with cold, dilute hydrochloric acid and extracted with ether. The ethereal solution was dried (Na_2SO_4), the solvent evaporated, and the residue washed twice with cold light petroleum (b. p. 30—50°). The 4-α-hydroxy-α-methylbenzyl-8-phenylsulphonyl-1-naphthol (2·5 g., 69%) obtained was filtered off and crystallised (cf. Table 1).

The *naphthols* listed in Table 1(*a*) were prepared similarly; except for methyl- and ethylmagnesium iodide the Grignard reagents used were bromides.

The naphthols dissolve in cold aqueous sodium hydroxide to give yellow solutions and their alcoholic solutions give an orange-red colour with ferric chloride; the same colour is given with concentrated sulphuric acid. In general, they dissolve in hot alcohol, benzene, and acetone, but are sparingly soluble in light petroleum (b. p. 40—60°).

Methylation was effected by ethereal diazomethane during 24 hours at 0°. The reaction mixture was evaporated; an ethereal solution of the residue was treated with aqueous potassium hydroxide (to remove unchanged naphthol), then with water, dried, and evaporated. The

TABLE 1*a*. 8-*Hydroxy*-1-*naphthyl Sulphones* (II).

R	R	M. p.	Solvent for crystn.	Found, % C	H	S	Active H	Formula	Required, % C	H	S	Active H	Colour in H_2SO_4
CMe_2·OH	Me	176°	A	60·0	5·5	11·0	—	$C_{14}H_{16}O_4S$	60·0	5·7	11·4	—	Yellow
CEtMe·OH	Et	158	A or C	62·1	6·4	10·2	0·60	$C_{16}H_{20}O_4S$	62·3	6·5	10·4	0·64	Orange-red
CPhMe·OH	Ph	168	C	71·0	4·8	7·8	0·46	$C_{24}H_{20}O_4S$	71·3	4·9	7·9	0·49	Orange
1-$C_{10}H_7$·CMe·OH	1-$C_{10}H_7$	163	D	75·9	4·6	6·0	—	$C_{32}H_{24}O_4S$ [a]	76·2	4·7	6·3	—	Orange-red
CPhMe·OH	Me	170	C	66·4	5·3	9·1	—	$C_{19}H_{18}O_4S$	66·7	5·2	9·4	—	Brown-red
CPhEt·OH	Et	181	C	67·9	5·6	8·4	0·52	$C_{21}H_{22}O_4S$	68·1	5·9	8·6	0·54	Red
CPh_2·OH	Ph	164	C	74·5	4·5	6·6	—	$C_{33}H_{22}O_4S$ [b]	74·7	4·7	6·9	—	Orange-red
CH_2Ph	Ph [1]	169	D	73·6	4·7	8·5	0·25	$C_{32}H_{18}O_3S$	73·8	4·8	8·5	0·26	Purple
1-$C_{10}H_7$·CH_2	1-$C_{10}H_7$	232	D	78·4	4·4	6·5	—	$C_{31}H_{22}O_3S$ [c]	78·5	4·6	6·8	—	Bluish-green

[a] Found: *M*, 498. Reqd.: *M*, 504. [b] Found: *M*, 452. Reqd.: *M*, 466. [c] Found: *M*, 460. Reqd.: *M*, 474.

[1] This experiment was carried out with A. F. A. Shalaby.

Solvents (all Tables): A, Ethyl alcohol; B, methyl alcohol; C, benzene–light petroleum (b. p. 40—60°); D, benzene; E, light petroleum (b. p. 100—110°).

TABLE 1*b*. *Methyl Ethers of* (II).

CMe_2·OH	Me	120°	C	61·0	5·8	10·7	—	$C_{15}H_{18}O_4S$	61·2	6·1	10·9	—	—
CEtMe·OH	Et	135	B	63·4	6·9	9·7	—	$C_{17}H_{22}O_4S$	63·3	6·8	9·9	—	—
CPhMe·OH	Ph	200	C	71·5	5·2	7·5	—	$C_{25}H_{22}O_4S$ [d]	71·8	5·3	7·6	—	—
1-$C_{10}H_7$·CMe·OH	1-$C_{10}H_7$	157	B	76·3	4·8	5·9	—	$C_{33}H_{26}O_4S$ [e]	76·4	5·0	6·2	—	—
CMePh·OH	Me	136	E	67·1	5·5	8·6	—	$C_{20}H_{20}O_4S$	67·4	5·6	9·0	—	—
CEtPh·OH	Et	142	E	68·5	6·2	8·1	—	$C_{22}H_{24}O_4S$	68·8	6·2	8·3	—	—
CPh_2·OH	Ph	150	B	74·7	5·0	6·5	—	$C_{30}H_{24}O_4S$ [f]	75·0	5·0	6·7	—	—
CH_2Ph	Ph	199	D	74·2	5·1	8·0	—	$C_{24}H_{20}O_3S$ [g]	74·2	5·1	8·0	—	—
1-$C_{10}H_7$·CH_2	1-$C_{10}H_7$	244	D	78·5	4·8	6·3	—	$C_{32}H_{24}O_3S$	78·7	4·9	6·5	—	—

[d] Found, OMe, 7·2. Reqd.: OMe, 7·4%. [e] Found: OMe, 5·8. Reqd.: OMe, 5·98%. [f] Found: OMe, 6·2. Reqd.: OMe, 6·5%. [g] Found: OMe, 7·8. Reqd.: OMe, 8·0%.

TABLE 2. 3-*Hydroxy*-2-*phenyl*-4 : 5-*benzo*-1 : 2-*thiazolines* (IX).

R	M. p.	Solvent for crystn.	Yield, %	Found, % C	H	N	S	Formula	Required, % C	H	N	S
Me	150°	A	75	69·0	5·3	5·6	12·9	$C_{14}H_{13}ONS$ [h]	69·1	5·3	5·8	13·2
Et	103	C	62	69·9	5·6	5·6	11·9	$C_{15}H_{15}ONS$ [i]	70·0	5·8	5·4	12·5
Ph	170	A	70	74·5	4·6	4·4	9·9	$C_{19}H_{13}ONS$	74·7	4·9	4·6	10·4

[h] Found: active H, 0·39. Reqd.: active H, 0·41%. [i] Found: active H, 0·35. Reqd.: active H, 0·39%.

TABLE 3. *Substituted* 4 : 5-*benzo*-1 : 2-*thiazoline* 1 : 1-*dioxides* (XII).

R	M. p.	Solvent for crystn.	Colour in H_2SO_4	Yield, %	Found, % C	H	N	S	Formula	Required, % C	H	N	S
Me	114°	C	Pale yellow	60	54·6	5·5	6·9	15·8	$C_9H_{11}O_2NS$	54·8	5·6	7·1	16·2
Et	144	D	Red	75	58·4	6·5	6·0	14·0	$C_{11}H_{15}O_2NS$	58·6	6·7	6·2	14·2
Pr^n	156	C	Yellow	65	61·5	7·3	5·5	12·4	$C_{13}H_{19}O_2NS$	61·7	7·5	5·5	12·6
Bu^n	72	B	Red	72	63·8	7·9	4·9	11·3	$C_{15}H_{23}O_2NS$	64·0	8·2	5·0	11·4

ethers prepared are recorded in Table 1(*b*). They are rather more soluble in organic solvents than are the parent naphthols.

Action of Grignard Reagents on N-Phenyl-o-sulphobenzoic Imide (V).—(a) *Phenylmagnesium bromide.* The imide (2 g.) (McClelland and Gait, *J.*, 1926, 921) was treated with phenylmagnesium bromide as detailed above. *N-Phenyl-o-sulphamyltriphenylcarbinol* (VI*a*) was obtained in colourless crystals (from benzene) (*ca.* 70%), m. p. 205° [Found: C, 72·4; H, 4·9; N, 3·3; S, 7·5; active H, 0·44%; *M* (Rast), 414. $C_{25}H_{21}O_3NS$ requires C, 72·3; H, 5·0; N, 3·4; S, 7·7; active H, 0·48%; *M*, 415]. It gives a brown colour with concentrated sulphuric acid, is soluble in hot benzene and ethyl alcohol, but difficultly soluble in light petroleum (b. p. 50—70°). The carbinol (0·5 g.) and ethereal diazomethane, as above, gave the *N-methyl* derivative (82%) as colourless crystals, m. p. 168° (Found: C, 72·6; H, 5·2; N, 3·3; S, 7·4. $C_{26}H_{23}O_3NS$ requires C, 72·7; H, 5·4; N, 3·3; S, 7·5%). It is easily soluble in benzene and alcohol, and gives an orange colour with concentrated sulphuric acid.

The carbinol (1 g.) was dissolved in concentrated sulphuric acid (5 c.c.) and set aside for 1 hour at room temperature. The red solution was heated on a water-bath for 30 minutes, poured into ice-water, and extracted with ether. The ethereal layer was washed with water, dried, and evaporated; the colourless crystals obtained were recrystallised from alcohol, and had m. p. 162° (Found: C, 70·6; H, 4·3; S, 9·8. Calc. for $C_{19}H_{14}O_3S$: C, 70·8; H, 4·3; S, 9·9%). The sulphonylide (VII) was identified by m. p. and mixed m. p. with an authentic specimen (List and Stein, *Ber.*, 1898, **31**, 1664). The aqueous layer was neutralised with sodium carbonate, extracted with ether, dried, and evaporated, and the oily residue was treated with benzoyl chloride in the presence of aqueous sodium hydroxide (10%). Benzanilide was obtained, m. p. and mixed m. p. 163°.

(b) *Methylmagnesium iodide.* The imide (V) (1 g.) was treated with methylmagnesium iodide (from magnesium, 0·6 g., methyl iodide, 3·6 g., and dry ether, 40 c.c.) as described previously. The oily residual *αα-dimethyl-o-N-phenylsulphamylbenzyl alcohol* (VI*b*) (75%) was washed several times with light petroleum (b. p. <50°) and crystallised from dilute alcohol as colourless crystals, m. p. 113—114° [Found: C, 61·6; H, 5·7; N, 4·6; S, 10·7%; *M* (Rast), 287. $C_{15}H_{17}O_3NS$ requires C, 61·9; H, 5·8; N, 4·8; S, 10·9%; *M*, 291]. The product is easily soluble in most organic solvents.

(c) *Ethylmagnesium iodide.* *αα-Diethyl-o-N-phenylsulphamylbenzyl alcohol* (VI*c*) (0·6 g.) was obtained similarly, by the action of ethylmagnesium iodide on (V) (1 g.), as colourless crystals (from ethyl alcohol), m. p. 117° (Found: C, 63·8; H, 6·5; N, 4·2; S, 9·8. $C_{17}H_{21}O_3NS$ requires C, 63·9; H, 6·6; N, 4·4; S, 10·0%). It is easily soluble in benzene, but difficultly soluble in light petroleum (b. p. <40°).

Action of Grignard Reagents on 2-Phenyl-4 : 5-benzo-1 : 2-thiazolone (VIII).—The results are given in Table 2.

3-Hydroxy-3-methyl-2-phenyl-4 : 5-benzo-1 : 2-thiazoline 1 : 1-Dioxide (X*a*).—To a solution of (IX*a*) (0·5 g.) in acetic acid (3 c.c.), hydrogen peroxide (1·5 c.c.) was added, and the reaction mixture was heated on a water-bath for 1 hour. On cooling, the colourless crystals that separated were recrystallised from alcohol; the *dioxide* had m. p. 155° (Found: C, 60·8; H, 4·6; N, 4·9; S, 11·5. $C_{14}H_{13}O_3NS$ requires C, 61·1; H, 4·7; N, 5·1; S, 11·6%). Yield *ca.* 88%.

The 2 : 3-*diphenyl* analogue (X*b*) was similarly obtained (79%) as colourless crystals (from acetic acid), m. p. 182° (Found: C, 67·3; H, 4·5; N, 3·9; S, 9·3. $C_{19}H_{15}O_3NS$ requires C, 67·6; H, 4·4; N, 4·2; S, 9·5%).

Action of Grignard Reagents on the Chloride (XI).—The chloride (2 g.) (Fritzsche, *loc. cit.*) was treated with phenylmagnesium bromide as detailed previously. 3 : 3-Diphenyl-4 : 5-benzo-1 : 2-thiazoline 1 : 1-dioxide (XII*e*) was obtained in colourless crystals (82%) (from benzene), m. p. 210° (Found: C, 71·0; H, 4·4; N, 4·3; S, 9·6. Calc. for $C_{19}H_{15}O_3NS$: C, 71·0; H, 4·7; N, 4·4; S, 9·9%). It was identified by the m. p. and mixed m. p. with an authentic specimen, prepared according to Fritzsche (*loc. cit.*). It gives a reddish-brown colour with concentrated sulphuric acid and dissolves in aqueous sodium hydroxide.

The dioxide (0·5 g.) and ethereal diazomethane give the 2-*methyl* derivative, m. p. 205° (from benzene) (Found: C, 71·5; H, 5·0; N, 3·9; S, 9·5. $C_{20}H_{17}O_3NS$ requires C, 71·6; H, 5·1; N, 4·2; S, 9·6%). This is easily soluble in hot benzene and alcohol, but difficultly soluble in light petroleum (b. p. 40—60°).

For *analogues* see Table 3.

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245. *Reactions with Benzoxanthones.*

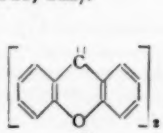
By Ahmed Mustafa and Mustafa Kamal Hilmy.

The preparation and the thermochromic behaviour of di-3 : 4- and -1 : 2-benzoxanthylidenes (II) and (III) are discussed. These substances are cleaved by sulphur at 270° to 3 : 4- and 1 : 2-benzoxanth-9-thione, and by oxalyl chloride, followed by water, to the corresponding benzoxanthones.

The action of phenylmagnesium bromide leads to 9-phenyl-3 : 4- and -1 : 2-benzoxanthhydrols, which on reduction yield 9-phenyl-3 : 4- and -1 : 2-benzoxanthenes.

Reduction of xanthones and the corresponding thioketones with lithium aluminium hydride gives the corresponding methanes.

Dixanthylidene (I) is almost colourless at low temperatures, but becomes bluish-green when heated and its hot solutions, *e.g.*, in anisole, are bluish-green (Schönberg and Schütz, *Ber.*, 1928, **61**, 478). We have studied the thermochromic behaviour of di-3 : 4- (II) and -1 : 2-benzoxanth-9-ylidene (III) (cf. Mustafa and Hilmy, *Science*, 1952, in the press). The former is pale yellow at room temperature, and green when molten, gives a bluish-green solution in warm anisole and, in general, exhibits remarkable thermochromic behaviour. The isomer, which forms yellowish-green crystals, melts to an olive-green liquid; its solutions, *e.g.*, in anisole, are more weakly thermochromic to the unaided eye than are solutions of (II). With both substances the reversibility of the thermochromic phenomenon is the same as with dixanthylidene (cf. Schönberg, Ismail, and Asker, *J.*, 1946, 442).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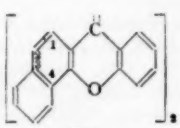
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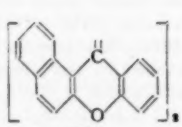
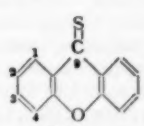

(III)


(IV)

The compounds (II) and (III) have been respectively obtained by the action of copper bronze on the 9 : 9-dichlorides from 3 : 4- and 1 : 2-benzoxanthone (cf. Schönberg and Asker, *J.*, 1942, 272) and by reduction of 3 : 4- and 1 : 2-benzoxanthone with zinc dust and acetic acid in the presence of concentrated hydrochloric acid (Gurgenjaz and Kostanecki, *Ber.*, 1895, **28**, 2310). The 3 : 4-benzo-compound has also been prepared by the action of copper bronze on 3 : 4-benzoxanth-9-thione (IV) (Schönberg, Schütz, and Nickel, *Ber.*, 1928, **61**, 1375).

Substances (II) and (III) behave remarkably towards sulphur and with oxalyl chloride. When heated with sulphur, they form thioketones, the reaction with (II) occurring in a few minutes at 270° (for mechanism see Schönberg, Ismail, and Asker, *loc. cit.*). Treatment with oxalyl chloride, followed by water, breaks the ethylene bond, giving 3 : 4- and 1 : 2-benzoxanthone (cf. Schönberg and Asker, *loc. cit.*).

3 : 4- and 1 : 2-Benzoxanthone react with phenylmagnesium bromide in the usual manner, giving 9-phenyl-3 : 4- and -1 : 2-benzoxanthhydrol respectively. These hydrols are reduced readily by zinc dust and acetic acid to 9-phenyl-3 : 4- and -1 : 2-benzoxanthen; their photochemical behaviour towards oxygen will be discussed later.

Conover and Tarbell (*J. Amer. Chem. Soc.*, 1950, **72**, 3586) have shown that 4 : 4′-dimethoxybenzophenone and *NN*-dialkylaminobenzophenone gave a considerable amount of 4 : 4′-dimethoxydiphenylmethane and *NN*-dialkylaminodiphenylmethane respectively, on reduction with lithium aluminium hydride. Xanthones, thioxanthone, and the two benzoxanthones with excess of lithium aluminium hydride give good yields of the xanthens.

Experimental

Di-3 : 4-benzoxanth-9-ylidene (II).—3 : 4-Benzoxanthone (2 g.) (Knapp, *J. pr. Chem.*, 1936, **146**, 116) was treated with oxalyl chloride (10 g.) (or with thionyl chloride, 15 c.c.) on a water-bath for 10 hours; the excess of oxalyl chloride was distilled off, and the residual orange oil

dissolved in dry xylene (30 c.c.) and refluxed with copper bronze (4 g.) for 6 hours with occasional shaking. The xylene solution was filtered hot and concentrated; on cooling, *di*-3 : 4-*benzoxanth*-9-*ylidene* separated in pale yellow crystals. It was filtered off, washed with cold acetone, and recrystallised from xylene; it (1·4 g.) had m. p. 346° (green melt), was sparingly soluble in boiling benzene and very sparingly so in absolute ethyl alcohol, and with concentrated sulphuric acid gave an orange-red colour [Found : C, 88·4; H, 4·2%; *M* (Rast), 450. $C_{34}H_{20}O_2$ requires C, 88·7; H, 4·35%; *M*, 460].

Reduction of 3 : 4-benzoxanthone (1 g.) with zinc dust (0·5 g.) and glacial acetic acid (10 c.c.) in the presence of concentrated hydrochloric acid (2—3 drops) gave *ca.* 0·05 g. of the same substance (identified by m. p. and mixed m. p. and thermochromic behaviour). This was also obtained by heating a mixture of copper bronze (2 g.) and 3 : 4-benzoxanth-9-thione (IV) (1 g.), in a stream of dry carbon dioxide, at 220° (bath-temp.) for 30 minutes. The xylene extract of the reaction mixture gave, on concentration, 0·5 g. of (II) (identified in the usual way).

Action of sulphur. The compound (II) (0·5 g.) was ground with sulphur (0·5 g.) and heated at 270° (bath-temp.) for 10 minutes, allowed to cool, powdered, and extracted repeatedly with light petroleum (b. p. 100—110°). The extract was concentrated, cooled, filtered from precipitated sulphur, further concentrated, and cooled. 3 : 4-Benzoxanth-9-thione crystallised in brown crystals, m. p. 140°, not depressed when mixed with a sample prepared as mentioned below.

Action of oxalyl chloride. The compound (II) (1 g.) was refluxed with oxalyl chloride (20 g.) for 6 hours, the excess of oxalyl chloride distilled off completely (pump), and the residual orange oil dissolved in benzene and shaken with water at 30° for 10 minutes. The benzene layer was evaporated and the residual pale yellow 3 : 4-benzoxanthone crystallised from benzene–light petroleum (b. p. 40—60°); it had m. p. 160° (Found : C, 82·8; H, 4·1. Calc. for $C_{17}H_{10}O_2$: C, 82·9; H, 4·1%) (m. p. and mixed m. p.); the mother-liquor also contained pure 3 : 4-benzoxanthone. The yield was almost quantitative.

Di-1 : 2-*benzoxanth*-9-*ylidene* (III).—This was prepared from 1 : 2-benzoxanthone (Graebe and Feer, *Ber.*, 1886, **19**, 2612; Kostanecki, *Ber.*, 1892, **25**, 1643) by the action of oxalyl chloride and copper bronze as described for the preparation of (II). It separated from the concentrated xylene solution, in yellowish-green crystals (*ca.* 75%), m. p. 290° (olive-green melt), soluble in hot xylene, difficultly soluble in alcohol and benzene. With concentrated sulphuric acid it gave an orange-red colour [Found : C, 88·5; H, 4·3%; *M* (Rast), 448. $C_{34}H_{20}O_2$ requires C, 88·7; H, 4·3%; *M*, 460]. It was also obtained, in *ca.* 15% yield, by the action of zinc dust and acetic acid in the presence of hydrochloric acid (cf. above).

Action of sulphur. 1 : 2-Benzoxanth-9-thione was obtained, by the action of sulphur on (III) as described in the case of (II), as green crystals (from benzene), m. p. 147° (m. p. and mixed m. p. with a sample prepared as described below).

Action of oxalyl chloride. The reaction was carried out as described in the case of (II) and the 1 : 2-benzoxanthone was obtained on crystallisation from benzene. It did not depress the m. p. of an authentic specimen (Graebe and Feer, *loc. cit.*).

3 : 4-*Benzoxanth*-9-*thione.*—The orange oil obtained by the action of oxalyl chloride (25 g.) on 3 : 4-benzoxanthone (5 g.), as described previously, was dissolved in dry benzene (40 c.c.) and refluxed for 6 hours with thiolacetic acid (8 c.c.), a deep green colour developing. The excess of benzene and acid was removed by distillation and, on addition of light petroleum (b. p. 40—60°) to the residue, 3 : 4-*benzoxanth*-9-*thione* was deposited in brown crystals (*ca.* 3·5 g.); recrystallised from benzene, it had m. p. 140—141° (Found : C, 77·6; H, 3·7; S, 12·2. $C_{17}H_{10}OS$ requires C, 77·9; H, 3·8; S, 12·2%). It dissolved in hot benzene to a greenish solution, was sparingly soluble in light petroleum and gave an orange-red colour with concentrated sulphuric acid. When mercuric chloride crystals were added to a dilute solution of it in benzene, they acquired a red-brown colour.

1 : 2-*Benzoxanth*-9-*thione.*—1 : 2-Benzoxanthone (4 g.), treated as above, gave this *thione* as dark green crystals (from benzene), m. p. 147° (green-melt) (*ca.* 2·6 g.) (Found : C, 77·7; H, 3·7; S, 12·1%). It was difficultly soluble in cold ether and soluble in concentrated sulphuric acid with a red colour. When the green solution of the substance in benzene was treated with mercuric chloride crystals, their colour changed immediately to red.

9-*Phenyl*-3 : 4-*benzoxanthen.*—To a Grignard solution of phenylmagnesium bromide [from magnesium (1·8 g.), bromobenzene (18 g.), and dry ether (75 c.c.)], dry benzene (40 c.c.) was added, and the mixture treated gradually with powdered 3 : 4-benzoxanthone (5 g.). The mixture was refluxed for 2 hours, set side overnight, poured into ice-cold, dilute hydrochloric acid, and extracted with ether, and the extract was dried and evaporated. The oily residue

solidified on storage and crystallised from benzene in colourless crystals, m. p. 230° (Found: C, 85·0; H, 4·7; active H, 0·29. $C_{25}H_{16}O_2$ requires C, 85·2; H, 4·9; active H, 0·31%). *9-Phenyl-3 : 4-benzoxanthhydrol* gave an orange-yellow colour with concentrated sulphuric acid, and was soluble in hot benzene, but slightly soluble in cold ethyl alcohol. Its reduction was carried out as described by Ullmann and Engi (*Ber.*, 1904, **37**, 2371) for 9-phenylxanthen by means of zinc dust and acetic acid with platinum chloride as a catalyst. *9-Phenyl-3 : 4-benzoxanthen* recrystallised from light petroleum (b. p. 80—100°) in colourless crystals, m. p. 133—134°, soluble in benzene and giving no colour with concentrated sulphuric acid (Found: C, 89·3; H, 5·2. $C_{25}H_{18}O$ requires C, 89·6; H, 5·2%).

9-Phenyl-1 : 2-benzoxanthen.—9-Phenyl-1 : 2-benzoxanthhydrol, obtained as described above, crystallised from alcohol in colourless crystals, m. p. 175—176° (Found: C, 85·1; H, 4·8; active H, 0·30%) (Dilthey, Quint, and Dahm, *J. pr. Chem.*, 1934, **141**, 75, gave for 9-phenyl-1 : 2-benzoxanthhydrol, m. p. 172—173°). Reduction, as described previously, gave 9-phenyl-1 : 2-benzoxanthen as colourless crystals (from benzene–ethyl alcohol), m. p. 169—170° (Found: C, 89·4; H, 5·2%); this gives no colour with concentrated sulphuric acid.

Reduction with Lithium Aluminium Hydride.—The reactions were carried out in solvents dried over sodium. A 250-c.c. three-necked flask fitted with a reflux condenser, mercury-sealed stirrer, and dropping funnel was used. To pulverised lithium aluminium hydride (0·5 g.) (from New Metals and Chemicals Ltd., London) was added ether (50 c.c.); stirring produced a milky suspension. After 15 minutes, 1 g. of the ketone or thioketone in benzene (40 c.c.) was added in portions. The reaction mixture was refluxed on a boiling water-bath for 3 hours with continuous stirring and then set aside overnight at room temperature. After addition to ice-cold water and treatment with aqueous ammonum chloride solution, the ethereal solution was washed with water, dried (Na_2SO_4), and evaporated; the reduction products are reported in the Table.

Reactant	Product *	Yield (%)	Reactant	Product *	Yield (%)
Xanthone	Xanthen	90	Michler's thioketone	Michler's methane ...	72
Thioxanthone	Thioxanthen	74	Xanthione	Xanthen	78
3 : 4-Benzoxanthone	3 : 4-Benzoxanthen [1]	85	Thioxanthione	Thioxanthen	83
1 : 2-Benzoxanthone	1 : 2-Benzoxanthen [2]	82	3 : 4-Benzoxanth-9-thione	3 : 4-Benzoxanthen...	81

[1] M. p. 95—96° [from light petroleum (b. p. 60—80°)] (Found: C, 87·8; H, 5·1. Calc. for $C_{17}H_{12}O$: C, 87·9; H, 5·2%); red picrate, m. p. 126° (Found: C, 59·8; H, 3·2; N, 9·0. Calc. for $C_{17}H_{12}O,C_6H_3O_7N_3$: C, 59·9; H, 3·3; N, 9·1%) (Baddar and Gindy, *J.*, 1951, **231**, have given for 3 : 4-benzoxanthen, m. p. 90—91°). [2] Colourless (from alcohol), m. p. 99—100° [Found: C, 87·7; H, 5·0%; *M* (Rast), 227. Calc. for $C_{17}H_{12}O$: C, 87·9; H, 5·2%; *M*, 232] (Phomina, *Annalen*, 1890, **257**, 89, gave for 1 : 2-benzoxanthen, m. p. 80°).

* The reduction products were identified by the m. p. and mixed m. p. with authentic specimens.

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246. *Lichens and Fungi. Part I. Polyporic Acid in* Stictae.

By J. MURRAY.

The lichens *Sticta coronata* and *S. colensoi* yield principally polyporic acid, calycin, pulvinic lactone, and neutral substances. The former species also contains pulvinic acid, two red quinonoid pigments, a phenol, and other substances.

Polyporic acid is the main pigment of the fungus *Peniophora filamentosa*.

AMONG the lichens, various species of *Sticta* (fam. *Stictaceae*) are notable for their yellow or orange colours. Nine members of the genus have been investigated by Zopf (*Annalen*, 1879, **297**, 271; 1899, **306**, 282; 1901, **317**, 110; 1904, **338**, 35), Hesse (*J. pr. Chem.*, 1900, **62**, 321), and Asano and Kamedo (*Ber.*, 1935, **68**, 1568), who found them to contain the orange-yellow pigment, stictaurin. No depsides appear to have been isolated from these lichens, although two species, *S.* (*Stictina*) *gilva* Thbg and *S. glaucolurida* Nyl. (Thies, in Klein's " Handbuch der Pflanzenanalyse," Vol. III, i, p. 434), yielded in addition to the pigment colourless neutral substances, stictinin and stictalbin respectively. From *S.*

coronata Muell. Arg. [*S. orygmaea* Ach. (?Hook.)], Zopf also obtained a brown, sparingly soluble pigment, "orygmaeic acid," m. p. 310°, which gave purple salts with alkalis. This substance has apparently not been reported since and nothing is known of its constitution, although Zopf suggested that it might be an anthraquinone.

During a recent investigation of New Zealand lichens, the pigments and other substances have been extracted from a number of *Stictae* including two related species, *S. coronata* Muell. Arg. and *S. colensoi* Bab. which yielded orygmaeic acid.

Sticta coronata, although yellow in texture, gives deep red solutions on extraction with organic solvents, being thus readily distinguished from *S. colensoi* Bab., *filix* Hoffm., *flavicans* Hook., *impressa* Hook., and *glaucolurida* Nyl. which are also yellow but give yellow solutions with ether or acetone. The dried plant gave a considerable yield of acetone-soluble material, from which were isolated orygmaeic acid (1·7%), calycin (3·2%), pulvinic lactone (0·7%), pulvinic acid (0·35%), compounds A (0·07%), B (0·02%), C (0·02%), and D (0·08%), and other substances (*ca.* 3%). Of these, compounds A and D are believed to be new, while pulvinic acid has apparently not been found previously in Nature, although the lactone and the methyl ester (vulpinic acid) have been isolated from many lichens.

"Orygmaeic acid" appeared to be identical with polyporic acid (2 : 5-dihydroxy-3 : 6-diphenylbenzoquinone) obtained from the fungus *Polyporus nidulans* Pers. by Stahlschmidt (*Annalen*, 1877, **187**, 177; cf. Kögl, *Annalen*, 1926, **447**, 78), and this was confirmed by direct comparison with an authentic specimen synthesized by the method of Shildneck and Adams (*J. Amer. Chem. Soc.*, 1931, **53**, 2373).

Compound A, a red pigment, is easily oxidised by air and has perhaps not been obtained completely pure. Analyses are best for a molecular formula $C_{14}H_{10}O_7$. At least three oxygen atoms are present as phenolic hydroxyl groups and two as a quinone group. The colour reactions of the substance are similar to those of anthragallol, but no recognisable product was obtained by zinc dust distillation and the pigment appears not to be an anthraquinone. It forms a neutral yellow acetate which is rapidly decomposed by sodium hydroxide to a mixture of colourless water-soluble products.

Compound B is also a hydroxy-quinone pigment, similar in general properties to compound A, but more stable to oxidation.

Compound D has properties typical of a group of about twenty neutral unreactive substances which have been isolated from lichens (see Thies in Klein's "Handbuch der Pflanzenanalyse," Vol. III, i). It is a colourless, highly crystalline substance, slightly soluble in most solvents, and optically active. It contains no methoxyl groups, shows no carbonyl or hydroxyl group reactions, and is unaffected by acid or alkali. Despite this lack of reactivity, the infra-red absorption spectrum has a strong carbonyl band at 1742 $cm.^{-1}$. There is no absorption corresponding to hydroxyl groups. Although there is a weak absorption band in the ultra-violet below 220 mμ, the substance appears to be saturated, and the infra-red spectrum shows no ethylenic absorption. Compound D may be a triterpenoid, but owing to our inability to prepare any derivatives of it, we have not yet been able to define accurately its molecular formula.

Sticta colensoi Bab. [*S. urvillea* Del. var. *colensoi* Nyl., *S. endochrysa* Fl. Ant., *S. durvillea* (Del) of Zahlbr.] gives about 5% of acetone extractives, comprising mainly polyporic acid and calycin with a small amount of pulvinic lactone. The red pigments of the previous species were absent; small amounts of two substances similar to compound D were obtained from the neutral fraction. Neutral substances identical with, or similar to, compound D have been isolated, sometimes in considerable yield, from several of the other *Sticta* species which have been examined.

In a search for polyporic acid from fungal sources, a considerable number of the available species belonging to the related genera *Polyporus* and *Fomes* were extracted. However, although fair yields of red and brown quinone-type pigments were obtained from a few species, none contained polyporic acid. The investigation was extended to fungi of the family *Thelephoraceae*, and from one of these, *Peniophora filamentosa* (B. & C.) Burt, polyporic acid was obtained in 5% yield. Preliminary tests of several other *Peniophora* and *Corticium* species (not yet identified) indicated the presence of pigments similar to polyporic acid, while descriptions in the botanical literature (*e.g.*, Burt, *Annals Missouri*

Bot. Gard., 1925, **12**, 213) suggest that pigments of this type may be widely distributed in these genera. It is perhaps worthy of note, however, that polyporic acid cannot be distinguished by simple colour tests from thelephoric acid, a phenanthraquinone pigment occurring in several members of the allied genus *Thelephora* (Zopf, *Bot. Zeit.*, 1889, **47**, 69) and in a lichen (Asahina and Shibata, *Ber.*, 1939, **72**, 153).

Experimental

Extraction of Sticta coronata.—The lichen, collected from trees at Port Pegasus, New Zealand, in January, was dried (450 g.) and extracted with warm acetone till the extracts were nearly colourless. The total extract was concentrated to about 150 c.c. and the crude crystallised pigments were filtered off, further small crops of calycin and polyporic acid being obtained by concentration of the filtrate. The crystalline material (25 g.) was extracted with the minimum amount of boiling acetone, leaving purple cubes of polyporic acid (7·2 g.). Stictaurin crystallised from this acetone extract as golden-yellow plates, m. p. 212°, followed by mixtures of calycin and pulvinic lactone in varying proportions and with m. p.s between 210° and 235°. These mixtures were separated by extracting a benzene solution with sodium hydrogen carbonate to remove traces of polyporic acid, then with very dilute sodium hydroxide solution which dissolved the calycin as the red sodium salt, leaving the pulvinic lactone in the neutral layer. Alternatively, the calycin–pulvinic lactone mixture was boiled with ethanol, which converted the lactone into ethyl pulvinate, leaving the calycin unchanged. The resulting mixture was readily separated by crystallisation from alcohol. The approximate yields of calycin and pulvinic lactone were 14·5 and 3 g. respectively.

The dark-red syrup (13 g.) obtained on evaporation of the first acetone mother-liquors was taken up in ether and extracted in turn with (*a*) aqueous sodium hydrogen carbonate and (*b*) aqueous sodium hydroxide, leaving (*c*) a straw-coloured neutral ethereal solution.

(*a*) The bicarbonate extract was acidified and extracted several times with ether. The extracted solution was still red, and on storage for several months slowly deposited a brown amorphous powder (250 mg.), charring above 370°, which has not been characterised. After removal of the ether, the syrupy residue was left in chloroform; a dark-brown semicrystalline material (i) slowly separated. This was removed and slow evaporation of the filtrate gave a crop of reddish-yellow powder (ii), followed by plates and small needles of *compound A* (240 mg.), and leaving a red syrup (iii).

Material (i) was extracted several times with warm acetone, leaving a residue of crude polyporic acid. Impure pigment B separated when the acetone extracts were cooled, and recrystallised from hot xylene as chocolate-brown plates (100 mg.). The xylene mother-liquors on further crystallisation yielded small amounts of polyporic acid, pigment B (5 mg.), and calycin (2 mg.).

The amorphous product (ii) (1·76 g.) was extracted (Soxhlet) with light petroleum to remove a little yellow oil, then a portion of it (1·15 g.) was boiled with ethanol, cooled, filtered to remove tarry material, diluted to 80% with water, and left for several days. The crystalline product which appeared gave orange-red needles of compound A (50 mg.) on recrystallization from 90% ethanol. The ethanolic mother-liquors were evaporated to a brown residue which was extracted with boiling light petroleum to remove a small amount of compound A. The insoluble residue (600 mg.) consisted of pulvinic acid. Alternatively, the mixture of compound A and pulvinic acid could be resolved by treatment with acetic anhydride and acetic acid at the b. p. The pulvinic acid was converted by this treatment into pulvinic lactone, and compound A formed a water-soluble yellow resin from which no useful material was obtained.

The syrup (iii), when kept in benzene, gave a crop of red amorphous material (220 mg.) and then was recovered as a pale reddish glass (3·0 g.). The latter gave a complex series of bands on alumina or magnesia, indicating the probable presence of five coloured substances, but the mixture could not be satisfactorily separated by chromatography. On sublimation up to 220°/0·02 mm. the only volatile products were about 30% of pulvinic lactone, m. p. 222° (ethyl ester, m. p. 127°), and traces of calycin, m. p. 245°, a white crystalline acid, m. p. 115°, a red liquid acid, and a liquid phenolic decomposition product. The pulvinic lactone is presumably derived from pulvinic acid in the crude material.

(*b*) The red-brown sodium hydroxide extract rapidly became purple, then black, on exposure to the air. On acidification it gave a black resin (3·0 g.) which was now partly soluble (1·1 g.) in sodium hydrogen carbonate solution. The remaining phenolic fraction crystallised from acetone as a white microcrystalline solid, m. p. 312° (90 mg.) (compound C). Evaporation of

the acetone mother-liquor gave a red-brown powder which could not be crystallized from any solvent. On treatment with acetic anhydride–acetic acid it formed a black insoluble neutral tar. Small amounts of calycin and acetylcalycin were obtained from the tar.

(*c*) The syrup obtained from the neutral ethereal solution gave white crystals of *compound D* (390 mg.) on slow evaporation of ethereal or methanolic solutions. The compound was then readily purified by crystallisation from hot alcohol. The bulk of the neutral fraction appeared as an amorphous, nearly colourless powder (*ca.* 4 g.) which has not been investigated.

Polyporic Acid.—The pigment was obtained as purple cubes from hot acetone, brown scales from xylene, or red needles from pyridine (losing pyridine on exposure to the air and falling to a brown powder), all of m. p. 315° (bath preheated to 310°). The m. p. determined in the ordinary way is 305—307° (decomp.). The spectrum in pyridine has maxima at 494 and 388 mμ (log ε 2·115 and 3·35), and the red solution becomes blue on dilution with water ($\lambda_{max.}$ 530 mμ). Zinc dust distillation gave a very poor yield of a non-picrate-forming hydrocarbon, m. p. 205°, presumably terphenyl. The diacetate was obtained in quantitative yield by refluxing the pigment with acetic anhydride and acetic acid for 30 minutes. It crystallised in yellow needles from benzene, or orange prisms from nitromethane, m. p. 212° (Found: C, 69·6; H, 4·1. Calc. for $C_{22}H_{16}O_6$: C, 70·2; H, 4·3%).

Synthetic polyporic acid was prepared by the route: benzoquinone, 2 : 5-diphenylbenzoquinone (25% yield), 2 : 5-diphenylquinol (80%), 2 : 5-dibromo-3 : 6-diphenylbenzoquinone (90%), polyporic acid (100%). Purification of the intermediate products was unnecessary. The spectrum of the synthetic sample was identical with those of the natural products, and the m. p.s and mixed m. p.s of the four samples of polyporic acid and their acetates were identical.

Calycin and Pulvinic Lactone.—Calycin was obtained as orange-red needles, m. p. 248°, from ethanol. Unlike pulvinic lactone, it is stable to prolonged boiling with alcohols. The acetate, prepared by refluxing of calycin in a large excess of acetic anhydride for 5 hours and cooling, separated as yellow needles (from ethanol or acetic acid), m. p. 179°. Pulvinic lactone crystallised in yellow needles, m. p. 227°, from benzene. The lactone, when heated under reflux in ethanol for 1 hour, gave pale yellow plates of the ethyl ester, m. p. 128°. The m. p. of ethyl pulvinate is only slightly depressed by admixture with calycin, both substances melting fairly distinctly close to their correct m. p.s.

Compound A.—The *compound* was obtained as small red needles (from chloroform), m. p. 227—228° [Found: C, 58·0; H, 4·1%; *M* (micro-electrometric titration), 294. $C_{14}H_{10}O_7$ requires C, 57·95; H, 3·45%; *M*, 290]. Crystallisation from 95% ethanol gave orange-red needles [Equiv., by microhydrogenation (one quinone group), 295±8], and from 10% ethanol–water, deep-red silky needles, m. p. 230° (decomp.) (Found: C, 54·2; H, 3·9. $C_{14}H_{10}O_7,H_2O$ requires C, 54·5; H, 3·9. The sample was dried *in vacuo* at room temperature). The compound is very soluble in ether and acetone and fairly soluble in other solvents, slightly so in light petroleum or water. It forms intense purple lakes on alumina and magnesia, from which it is not readily recovered in a crystalline state. The solution in acetic acid is orange-red (impure specimens may give a slight greenish fluorescence); in sodium hydrogen carbonate solution, it is dark greenish-purple (absorption bands in blue and yellow regions), in dilute ammonia green (becoming red, then brown), in sodium hydroxide blue-purple (rapidly bleaching in air), and in concentrated sulphuric acid yellow-brown (unchanged by addition of boric acid). It gives a deep greenish-brown colour with ferric chloride. The pK_a values are 5·8 (green), 7·5 (blue), and *ca.* 10 (purple). Its absorption max. (mμ) and log ε in various solvents are tabulated.

EtOH (abs.) ...	—	502	474	—	337	—	—
Dioxan	—	—	—	—	337	274	244
EtOH (90%) ...	—	520	470	—	340	272	241
	—	3·64	3·696	—	3·828	4·240	4·192
4N-NaOH	675—650	580	500	402	314	261·5	—
	3·46	3·60	3·57	3·42	4·04	4·20	—
H_2SO_4	650—630	518	483·5	—	288·5	—	—
	(3·0)	3·975	3·734	—	4·065	—	—
H_2SO_4–B_2O_3 ...	675—630	522	487	462 (infl.)	290·5	—	—
	(3·2)	4·314	4·094	3·867	4·466	—	—

Distillation of the pigment with zinc dust gave a very small yield of a white volatile substance, m. p. 20—25°, which did not form a picrate.

Acetate. Attempted acetylation with acetic anhydride or acetyl chloride in the presence of sulphuric acid, sodium acetate, or pyridine led to yellow water-soluble tars. Compound A

(34 mg.) was kept in cold acetic anhydride (0·5 c.c.) with 1 drop of 60% perchloric acid for 1 hour, then poured into cold water. The resulting orange *triacetate* (25 mg.) crystallised from ethanol–acetic acid as yellow needles, m. p. 193—194° (decomp.) [Found: C, 57·2; H, 3·4%; *M* (microhydrogenation), *ca.* 380. $C_{26}H_{16}O_{10}$ requires C, 57·6; H, 3·85%; *M*, 416. The molecular weight from microhydrogenation is probably low, owing to partial hydrogenolysis, as the recovery of the acetate from the leuco-compound was not quantitative]. The spectrum of the acetate in 90% ethanol showed maxima at 360, 300, 263, and 230 mμ.

A substance which may be the acetate of the leuco-compound was prepared by treatment of the compound A with zinc dust in acetic anhydride and acetic acid. It separated from ethanol–acetic acid as pale fawn-coloured needles, m. p. 105—107° (decomp.), but has not been obtained pure.

Compound B.—The chocolate-coloured plates (from xylene) melted indefinitely with decomposition at 335—340°. *B* was obtained as red needles, m. p. 330—340°, from ethanol. The m. p. was not improved by repeated recrystallisation from xylene or toluene, and it could not be satisfactorily crystallised from other solvents. It gives blood-red solutions in oxygenated solvents, brown ones in aromatic hydrocarbons, and is insoluble in light petroleum or water. The compound formed a deep violet band on alumina or magnesia, which could be eluted only with glacial acetic acid. This did not effect any resolution and the properties of the substance were unchanged on recovery. The solution in acetic acid is bright red, in aqueous sodium hydrogen carbonate red, in sodium hydroxide purple (red in very dilute solution and stable to aerial oxidation), in sulphuric acid violet, and in sulphuric–boric acid purple. The spectra of the last two solutions (to be reported later) are markedly different. Compound B gives a dark green colour with ferric chloride.

Pulvinic Acid.—The compound was obtained as large brown crystals from ethanol, falling to a yellow powder, m. p. 215°, on exposure to the air. Volhard (*Annalen*, 1894, **282**, 1) gives m. p. 215—216° for synthetic pulvinic acid (Found, in a sample dried at 100°: C, 70·0; H, 4·4. Calc. for $C_{18}H_{12}O_5$: C, 70·1; H, 3·9%). Pulvinic acid gives yellow solutions in alkalis and orange, fading to yellow, ones in concentrated sulphuric acid. It gives no colour with ferric chloride and does not reduce silver nitrate. Refluxing the compound with excess of acetic anhydride for 1 hour gave a quantitative yield of pulvinic lactone, m. p. 220° (Found: C, 73·9; H, 3·6. Calc. for $C_{18}H_{10}O_4$: C, 74·4; H, 3·5%). The m. p. could not be raised by crystallisation, but a mixture with pulvinic lactone, m. p. 226°, had m. p. 223°, and a sample was converted into ethyl pulvinate, m. p. 127°.

Compound D.—The *compound* was obtained as glistening white plates, m. p. 259°, from methanol or ethanol [Found, in a sample dried at 100°/0·01 mm.: C, 72·4; H, 9·4%; *M* (Rast), 525, 535. $C_{32}H_{50}O_6$ requires C, 72·45; H, 9·4%; *M*, 530. $C_{34}H_{48}O_6$ requires C, 72·0; H, 9·3%; *M*, 516]; it had $[\alpha]_D^{18}$ +54° (*c*, 0·02 in dioxan). The ultra-violet spectrum shows an apparent maximum at 216 mμ (ε *ca.* 220). The absorption in dioxan at 220 mμ is 190; at 230 mμ, ε is 100; and at 270—280 mμ, ε is *ca.* 9. Compound D is moderately soluble in dioxan and acetone, slightly in most other solvents except water. It was recovered unchanged after being heated with acetic anhydride in acetic acid or pyridine for 4 hours, or with boiling alcoholic or 50% aqueous potassium hydroxide at 150°. It did not react with semicarbazide or dinitrophenylhydrazine. It was not hydrogenated in presence of Adams's catalyst in glacial acetic acid, did not absorb bromine, and gave no colour with tetranitromethane. The compound was insoluble in cold concentrated sulphuric acid but dissolved on warming to an orange solution with bright green fluorescence. The Liebermann–Burchard reaction gave an immediate violet-red colour, fading to yellow after 3 hours. The infra-red spectrum (in Nujol) shows absorption (in $cm.^{-1}$) at 1742 (vs), 1296 (m), 1258 (s), 1240 (vs), 1190 (m), 1156 (w), 1105 (w), 1081 (w), measured on a Perkin–Elmer Model 21 instrument.

Extraction of S. colensoi (with G. A. Nicholls, Canterbury University College).—The plant (collected in the Waimakariri Valley, N.Z.) was extracted essentially as for *S. coronata*, giving polyporic acid (1·2%), calycin (3·2%), pulvinic lactone (0·2%), and colourless neutral substances (0·3%).

Extraction of Peniophora filamentosa.—This species is not uncommon in the north temperate zone, but has apparently not been reported previously from New Zealand. The whole dried plant (10 g.) (collected from a dead branch in March) was extracted with boiling ether for 8 hours. Polyporic acid (0·53 g.) crystallised from the hot solution and was filtered off. The filtrate on concentration gave brown and purple plates (20 mg.), then a yellow oil from which a trace of white wax, m. p. *ca.* 40°, slowly separated. The second crop of pigments was refluxed with acetic anhydride–acetic acid for 10 minutes; when the mixture cooled, grey-brown scales,

m. p. 360° (decomp.) (12 mg.), crystallised, leaving the contaminating polyporic acid in solution as the diacetyl derivative. This grey substance crystallises from pyridine as a violet-brown salt but was not otherwise characterised.

The author is indebted to Dr. T. S. Ma, Microchemical Laboratory, for most of the micro-analyses, to Dr. R. N. Haszeldine for an infra-red spectrographic determination, and to the Director, Royal Botanical Gardens, Kew, for the identification of *Peniophora filamentosa*.

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247. *2-Mercaptoglyoxalines. Part VI.* The Preparation of Mono- and Di-carbon-substituted 2-Mercaptoglyoxalines by Means of the Dakin and West Reaction.*

By R. A. F. BULLERWELL and ALEXANDER LAWSON.

Several α-amino-ketones have been formed by the Dakin and West reaction and condensed with thiocyanate to give 4-mono- and 4 : 5-di-alkyl-substituted 2-mercaptoglyoxalines. An improved method for the preparation of 3-benzamido-1-benzoyl-2 : 4-diketopyrrolidine (Rügheimer, *Ber.*, 1889, **22**, 1954), and a new method for preparation of 1 : 4-dihydroxy*iso*quinoline, are described.

EXCEPT for methods of rather limited application, such as the condensation of thiourea with α-hydroxy-ketones including benzoin (Basse and Klinger, *Ber.*, 1898, **31**, 1217) and *o*-diamines, the isomerisation of 2-acylamino-5-aminothiazoles (Cook and Heilbron, *J.*, 1948, 1262), and the condensation of *S*-benzyl*iso*thiourea and phenacyl bromide followed by fission of the benzyl group (Dodson, *J. Amer. Chem. Soc.*, 1948, **70**, 2753), methods available for the preparation of 2-mercaptoglyoxalines depend on the reaction between thiocyanate with α-amino-aldehydes and -ketones. Synthesis of the last-named compounds therefore is the main problem associated with the preparation of the 2-mercaptoglyoxalines.

Dakin and West (*J. Biol. Chem.*, 1928, **78**, 91, 745, 757) showed that many α-amino-acids give acetamidomethyl ketones and carbon dioxide when heated with pyridine and acetic anhydride, though with glycine and hippuric acid low yields prohibited the useful application of the products. From the corresponding amino-ketones obtained on hydrolysis, they prepared the three 2-mercaptoglyoxalines derived from phenylalanine, tyrosine, and phenylglycine severally.

We have employed the Dakin and West reaction with acetic and propionic anhydrides to prepare six typical 4 : 5-dialkyl-substituted 2-mercaptoglyoxalines. By use of the technique adopted by Attenburrow, Elliott, and Penny (*J.*, 1948, 310) for the preparation of benzamidoacetone, acetic, propionic, butyric, and hexanoic anhydrides have been condensed with sodium hippurate to give the corresponding oxazolones from which the appropriate 4-substituted 2-mercaptoglyoxalines have been isolated after hydrolysis and treatment with thiocyanate. This method gave smaller yields than that obtainable by the Akabori reduction of amino-acid esters (Bullerwell and Lawson, *J.*, 1951, 3030). The yields diminished with increasing molecular weight of the anhydride.

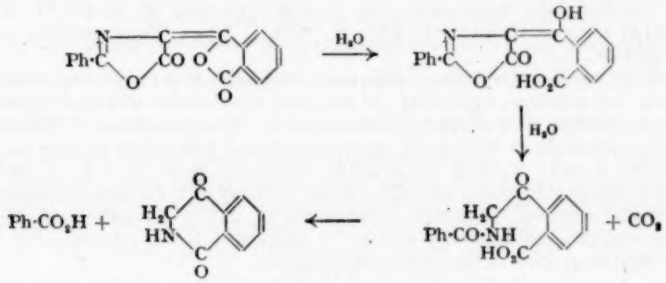
Attempts to prepare γ-keto-ornithine by the action of aspartic acid chloride azlactone on 2-phenyloxazolone were not successful. The only crystalline product isolated from the reaction was 3-benzamido-1-benzoyl-2 : 4-diketopyrrolidine, obtainable in much better yield (40%) by simply allowing 2-phenyloxazolone to stand in 2-picoline overnight. The structure of this substance, originally obtained by Rügheimer (*Ber.*, 1888, **21**, 3325; 1889, **22**, 1954), was established by Cornforth and Huang (*J.*, 1948, 1958). The formation of Rügheimer's compound may be regarded as a special case of the Dakin and West re-

* Part V, *J.*, 1951, 3030.

action in which the second oxazolone molecule behaves in a manner analogous to that of an acid anhydride.

It is possible that the compound, obtained by Attenburrow *et al.* (*loc. cit.*) from benzoyl-α-alanine and acetic anhydride, which gave analyses for $C_{20}H_{18}O_4N_2$ and for which a diketopiperazine structure was suggested, is the dimethyl homologue of Rügheimer's compound. One would expect the two molecules of 4-methyl-2-phenyloxazol-5-one to condense in the same manner as the unmethylated compound. 3-Benzamido-1-benzoyl-2 : 4-diketopyrrolidine on hydrolysis and treatment with potassium thiocyanate gave 4-aminomethyl-2-mercaptoglyoxaline, but it was not possible to develop this into a convenient preparative method for the latter substance.

Efforts to apply the Dakin and West reaction to aliphatic dibasic acid anhydrides were not successful. The only known examples of oxazolone synthesis of this kind are described by Erlenmeyer (*Annalen*, 1893, **275**, 1) who obtained 2-phenyl-4-phthalidylideneoxazol-5-one using phthalic anhydride, and by Smith and Hanna (*J. Amer. Chem. Soc.*, 1951, **73**, 2387) who used 3-nitrophthalic anhydride to make the corresponding nitro-derivative. Substituting sodium hippurate for the mixture of hippuric acid and sodium acetate, we obtained the pure oxazolone in much improved yield, in keeping with the findings of Attenburrow *et al.* (*loc. cit.*) that acetic acid had a deleterious effect on oxazolone formation. Subsequent hydrolysis of the oxazolone gave rise to 1 : 4-dihydroxy*iso*quinoline, the formation of which may be explained by the following mechanism.



Experimental

2-Phenyl-4-1′-hydroxyalkylideneoxazol-5-ones.—2-Phenyl-4-1′-hydroxyethylideneoxazol-5-one and 2-phenyl-4-1′-hydroxypropylideneoxazol-5-one were prepared by the method of Attenburrow *et al.* (*loc. cit.*) adapted for use on a small scale. Two more analogues were prepared in a similar way.

Sodium hippurate (20 g., 0·1 mole), 2-picoline (30 ml.), and butyric anhydride (48 ml., 0·3 mole) were stirred together for 3 hours in a three-necked flask fitted with a calcium chloride tube and warmed to 35°. The liquid so obtained was filtered and excess of butyric anhydride was decomposed by stirring with ethanol (17 ml.) and cooling in water. Water (170 ml.) was then added and the solution was made acid to Congo-red with 5N-hydrochloric acid (100 ml.) while stirring and cooling were continued. The solid precipitate was filtered off and dissolved in hot N-sodium hydroxide at 80°, and charcoal (1 g.) added, with stirring for 15 minutes. The filtrate was then cooled and acidified. The precipitate, of *4-1′-hydroxybutylidene-2-phenyloxazol-5-one*, after being filtered off, dried (yield, 17·5 g., 75%), and recrystallised from ethyl acetate, had m. p. 169° (Found : C, 67·5; H, 5·6. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·6%).

Sodium hippurate (20 g.), 2-picoline (30 ml.), and hexanoic anhydride (70 ml.) were brought into reaction as described above. *4-1′-Hydroxyhexylidene-2-phenyloxazol-5-one*, m. p. 129° (2·6 g., 10%), was obtained (Found : C, 69·1; H, 6·4. $C_{15}H_{17}O_3N$ requires C, 69·5; H, 6·6%).

Alkyl Benzamidomethyl Ketones.—By following the directions of Attenburrow *et al.*, benzamidoacetone was obtained from 4-1′-hydroxyethylidene-2-phenyloxazol-5-one by boiling water. Two more benzamidomethyl ketones were obtained in this way. It was, however, more satisfactory in the case of 4-1′-hydroxyhexylidene-2-phenyloxazol-5-one to omit the isolation of the benzamido-ketone and carry out the complete hydrolysis in one stage with dilute hydrochloric acid.

4-1′-Hydroxypropylidene-2-phenyloxazol-5-one (10 g.) was boiled in distilled water (600 ml.) for 1 hour and the yellow solution was evaporated to dryness under reduced pressure. The residue (8·0 g., 97%) was *benzamidomethyl ethyl ketone*, m. p. 68° (Found: C, 68·0; H, 6·9. $C_{11}H_{13}O_3N$ requires C, 69·1; H, 6·8%).

4-1′-Hydroxybutylidene-2-phenyloxazol-5-one (10 g.), treated as above, gave *benzamidomethyl propyl ketone*, m. p. 63° (95%) (Found: C, 69·3; H, 7·2. $C_{12}H_{15}O_3N$ requires C, 70·2; H, 7·3%).

2-*Phenyloxazolone*.—Considerable difficulty was encountered in the preparation of 2-phenyloxazolone by the method of Abbot ("Chemistry of Penicillin," Princeton Univ. Press, 1949, p. 778) but the following procedure was satisfactory.

Hippuric acid (100 g.) and acetic anhydride (300 ml.) were stirred together and heated on the steam-bath until all dissolved. The orange-coloured solution was then immediately cooled to room temperature, filtered, and evaporated to dryness *in vacuo* at 25—30°/0·1 mm. The semi-solid residue was twice ground thoroughly with cold ethanol with filtration between grindings. The solid was finally washed on the funnel with cold ethanol and dried *in vacuo* over activated alumina. The yield was 41 g. (45·5%), and the m. p. 91°.

3-*Benzamido*-1-*benzoyl*-2 : 4-*diketopyrrolidine*.—2-Phenyloxazol-5-one (20 g.) was dissolved in 2-picoline (50 ml.) and set aside for 48 hours in the refrigerator. The dark red solution was then poured on crushed ice, and, with stirring, dilute hydrochloric acid was added until the whole was just acid to Congo-red. The precipitate was filtered off and triturated with water. After draining at the pump and washing with a little cold ethanol, crude 3-benzamido-1-benzoyl-2 : 4-diketopyrrolidine (8 g., 40%) was obtained. This was recrystallised from a mixture of ethanol and water as the *hemihydrate*, m. p. 116° (Found: C, 65·5; H, 4·8; N, 8·3. $C_{18}H_{14}O_4N_2,\frac{1}{2}H_2O$ requires C, 65·3, H, 4·5; N, 8·5%). Upon losing water it solidified and melted again at 139°.

3-*Benzamido*-2 : 4-*diketopyrrolidine*.—3-Benzamido-1-benzoyl-2 : 4-diketopyrrolidine (5 g.) was dissolved in hot N-sodium hydroxide (50 ml.), and the solution was kept at 80° for ½ hour, then cooled and acidified with dilute hydrochloric acid. The precipitate of 3-benzamido-2 : 4-diketopyrrolidine obtained in 95% yield and recrystallised from ethyl acetate had m. p. 205° (Found: C, 60·5; H, 4·5; N, 12·6. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6; N, 12·7%).

Boiling with acetic anhydride, according to the method of Cornforth and Huang (*loc. cit.*), gave 3-acetamido-1-acetyl-2 : 4-diketopyrrolidine, m. p. 218°. Hydrolysis of this compound (see below) did not proceed smoothly enough to make it a better alternative to the benzoyl derivative for the preparation of the mercaptoglyoxaline.

Hydrolyses.—The above benzamido-ketones, 4-1′-hydroxyhexylidene-2-phenyloxazol-5-one, and 3-benzamido-2 : 4-diketopyrrolidine were hydrolysed and the amino-ketones without isolation were condensed with thiocyanate to give the corresponding mono-carbon-substituted *mercaptoglyoxalines*. One typical example is described and the results are summarised in Table 1 (crystallisation from water, except for the amyl compound from benzene–light petroleum).

Benzamidoacetone (4 g.) was refluxed for 3 hours with 20% hydrochloric acid (50 ml.). The solution was then cooled, filtered from benzoic acid, and evaporated under reduced pressure. The solid residue was washed with ether and dissolved in water (20 ml.). Ammonium thiocyanate (5 g.) was added and the solution was boiled under reflux for ½ hour. On cooling, 1·5 g. of 2-mercapto-4-methylglyoxaline (m. p. 246°) separated.

TABLE 1. 4-*Substituted* 2-*mercaptoglyoxalines*.

			Found, %					Required, %			
Substituent	Yield, %*	M. p.	C	H	N	S	Formula	C	H	N	S
Me	45	246°	—	—	—	—	$C_4H_6N_2S$	—	—	—	—
Et	40	165	47·0	6·4	—	—	$C_5H_8N_2S$	46·9	6·3	—	—
Pr	36	183	50·7	6·9	—	—	$C_6H_{10}N_2S$	50·7	7·0	—	—
C_5H_{11}	6	111	—	—	—	—	$C_8H_{14}N_2S$	—	—	—	—
$CH_2{\cdot}NH_2,HCl$	8	—	29·2	4·8	25·3	18·9	$C_4H_9N_2SCl$	29·0	4·8	25·4	19·3

* Based on sodium hippurate or phenyloxazolone.

Disubstituted 2-*Mercaptoglyoxalines*.—The 4 : 5-di-carbon-substituted mercaptoglyoxalines from amino-acids and acid anhydrides were prepared by Dakin and West's reaction (*loc. cit.*), *viz.*: 4-ethyl-2-mercapto-5-methylglyoxaline from DL-alanine, 4-*ethyl*-2-*mercapto*-5-*propylglyoxaline* from DL-norvaline, 4-*benzyl*-5-*ethyl*-2-*mercaptoglyoxaline* from DL-phenylalanine,

4-*ethyl*-5-p-*hydroxybenzyl*-2-*mercaptoglyoxaline* from L-tyrosine, and **4-(4-*hydroxy*-3 : 5-*di-iodophenoxymethyl*)-2-*mercapto*-5-*methylglyoxaline*** from DL-3 : 5-di-iodothyronine. The method is illustrated by the following example and Table 2 summarises the work.

DL-Alanine (10 g.), pyridine (25 ml.), and acetic anhydride (60 ml.) were heated together on the steam-bath until evolution of carbon dioxide had ceased. (In other cases an oil-bath at 150° was required.) Water (200 ml.) was then added and the mixture was steam-distilled until most of the pyridine was removed. After the solution had been made just alkaline with sodium carbonate, a further short steam-distillation was required to remove the remaining pyridine. The solution was then made acid to Congo-red and concentrated to 50 ml. An equal volume of concentrated hydrochloric acid was added and the solution was refluxed for ½ hour. After concentration nearly to dryness, the residue was dissolved in water, and ammonium thiocyanate (27 g.) added. The solution was boiled for 1 hour. On cooling, 7·5 g. of 2-mercapto-4 : 5-dimethylglyoxaline separated. It did not melt below 300°.

TABLE 2. 4-R-5-R'-2-*mercaptoglyoxalines.*

		Yield,			Found, %				Required, %		
R	R'	%	M. p.	Solvent	C	H	N	Formula	C	H	N
Me	Me	40	—	EtOH	47·2	6·6	—	$C_6H_8N_2S$	46·9	6·3	—
Me	Et	26	—	,,	50·9	6·7	20·0 §	$C_6H_{10}N_2S$	50·7	7·0	19·7
Pr	Et	22	297° ‡	,,	56·6	8·1	—	$C_8H_{14}N_2S$	56·5	8·2	—
CH_2Ph *	Et	27	252	,,	65·9	6·3	—	$C_{13}H_{14}N_2S$	66·0	6·4	—
p-OH·C_6H_4·CH_2 *	Et	25	282 ‡	Aq. EtOH	61·1	5·9	—	$C_{13}H_{14}ON_2S$	61·5	6·0	—
X * †	Me	21	—	Aq. AcOH	36·1	2·7	4·6	$C_{17}H_{14}O_2N_2SI_2$	36·2	2·5	5·0

X = 4-*p*-Hydroxyphenoxy-3 : 5-di-iodobenzyl.

* The corresponding acylamino-ketones could be extracted with ether, thus eliminating the steam-distillation.

† Owing to the insolubility of the amino-ketone hydrochloride, the condensation with thiocyanate was carried out in ethanol–water (1 : 1).

‡ With decomp. § Found : S, 22·5. Reqd. : S, 22·5%.

2-*Phenyl*-4-*phthalidylideneoxazol*-5-*one*.—Phthalic anhydride (15·7 g.), sodium hippurate (20 g.), and acetic anhydride (40 ml.) were heated together on the steam-bath for 3 hours with continual stirring. The mixture was then cooled and the solid filtered off, rubbed with ethanol (2 ml.), and drained. The solid was ground and washed with water (100 ml.) in portions. The product (20 g., 70%) had m. p. 242° (Erlenmeyer, *loc. cit.*, gives 240°). Recrystallisation was unnecessary.

1 : 4-*Dihydroxyisoquinoline*.—2-Phenyl-4-phthalidylideneoxazol-5-one (16 g.), dissolved in hot N-sodium hydroxide (250 ml.), was kept at 80° for ½ hour, then cooled and acidified with dilute hydrochloric acid. The precipitate (15·5 g.) was filtered off and refluxed for 2½ hours with 20% hydrochloric acid (200 ml.). Benzoic acid was then removed by steam-distillation. The solution was concentrated under reduced pressure and the 1 : 4-dihydroxy*iso*quinoline (5·3 g., 60%) separated. It reddened at >200° and did not melt. For identification the **4-*acetate*** (m. p. 207°) was prepared (Gabriel and Colman, *Ber.*, 1902, **35**, 2421) (Found : C, 64·9; H, 4·4. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·4%).

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248. *Experiments on the Synthesis of Santonin. Part I. The Preparation of the Lactone of α-(2-Hydroxy-3-ketocyclohexyl)propionic Acid.*

By F. D. Gunstone and R. M. Heggie.

The lactone of α-(2-hydroxy-3-ketocyclohexyl)propionic acid, an intermediate required for the synthesis of santonin, has been prepared. It has not been possible to relate this lactone to any known compound but indirect evidence suggests that the crystalline product has, in fact, the structure stated.

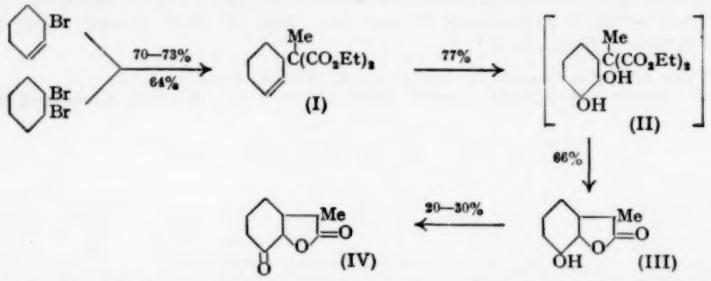
Mitchell and his co-workers (*J.*, 1939, 889; 1947, 686) suggested that *rac.*-parasantonide would be suitable for asymmetric photochemical work with wave-lengths around 3000 Å. It was concluded (Mitchell and Scott, unpublished work) that since racemisation of santonin, santonic acid, or parasantonide is impracticable, *rac.*-parasantonide could be best obtained from *rac*-santonin, the synthesis of which is the object of the present work. The structure of santonin is known from the work of Clemo *et al.* (*J.*, 1930, 1110, 2579).

The synthesis of santonin and related compounds claimed by Paranjape, Phalnikar, Bhide, and Nargund (*Rasayanam*, 1943, I, 233; *Chem. Abs.*, 1944, **38**, 4266; *Proc. Ind. Acad. Sci.*, 1944, A, **19**, 381; *Nature*, 1944, **153**, 141) has been much criticised for various reasons (Clemo, Cocker, and Hornsby, *J.*, 1946, 616; Wilds and Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1715; Martin and Robinson, *J.*, 1949, 1867; Cornforth, Cornforth, and Dewar, *Nature*, 1944, **153**, 317; O'Gorman, *J. Amer. Chem. Soc.*, 1944, **66**, 1041; Woodward and Singh, *ibid.*, 1950, **72**, 494; Heggie, Thesis, Glasgow, 1951). So far as the authors are aware no reply has been made. Another report of a projected synthesis of santonin (Banerjea, *Science and Culture*, 1948, **13**, 347; *Chem. Abs.*, 1948, **42**, 5890) describes work which has not been completed.

The present attempt to synthesise santonin is being developed in three stages, *viz.*, (i) synthesis of the lactone (IV) of α-(2-hydroxy-3-ketocyclohexyl)propionic acid, (ii) an investigation into methods of preparing the dienone system present in santonin, and (iii) an attempt to apply these methods to the appropriate methylated keto-lactone required to yield santonin. This paper is an account of the preparation of the keto-lactone (IV).

The claim by Paranjape *et al.* (*loc. cit.*) to have prepared (IV) in "fairly moderate yield" by condensation of 3-chlorocyclohex-2-enone with ethyl methylmalonate and subsequent hydrolysis has been questioned by Clemo, Cocker, and Hornsby (*loc. cit.*) and by Carruthers and Mitchell (private communication), each of whom obtained 3-ethylcyclohex-2-enone in high yield by this procedure.

The preparation described in this paper is illustrated in the annexed scheme. Diethyl α-cyclohex-2-enyl-α-methylmalonate (I) was obtained by condensation of 1 : 2-dibromo-



cyclohexane with diethyl methylmalonate in presence of 2 mols. of sodium ethoxide (Mousseron and Winternitz, *Bull. Soc. chim.*, 1946, **13**, 604), or from 3-bromocyclohexene (Ziegler, Späth, Schaaf, Schumann, and Winkelmann, *Annalen*, 1942, **551**, 109) in a similar condensation using 1 mol. of sodium ethoxide. The former method was preferred, despite the lower yield, because the dibromide was more readily available. The two products gave the same substituted malonic acid [m. p. 158° (decomp.)] on hydrolysis. Mousseron and Winternitz (*loc. cit.*) however give 137° as the melting point of this compound, and Kon and Speight

(*J.*, 1926, 2727) have described α-*cyclo*hex-1-enyl-α-methylmalonic acid (m. p. 155°) which they prepared by condensation of *cyclo*hexanone with malonic ester with subsequent methylation and hydrolysis. The condensation used by Mousseron and Winternitz and by us has been utilised by many authors for the preparation of substituted malonic esters containing the *cyclo*hex-2-enyl or other similar cyclic group (Eikmann, *Chem. Centr.*, 1909, II, 2146; Miescher and Hoffmann, *Helv. Chim. Acta*, 1941, **24**, 458; Buu-Hoï and Cagniant, *Bull. Soc. chim.*, 1942, **9**, 99; Moffett, Hart, and Hoehn, *J. Amer. Chem. Soc.*, 1947, **69**, 1849, 1854; Fieser *et al.*, *ibid.*, 1948, **70**, 3195). We have repeated the experiments of Kon and Speight (*loc. cit.*) and have shown that the product so obtained differs from ours by comparison of the barbiturates, the substituted malonic acids, and the amides of the corresponding monobasic acids. We therefore conclude that the figures given by Mousseron and Winternitz are in error.

Performic acid (Swern, Billen, Findley, and Scanlan, *J. Amer. Chem. Soc.*, 1945, **67**, 1786; English and Gregory, *ibid.*, 1947, **69**, 2120) was the most convenient reagent for oxidation of the unsaturated ester to the glycol (II) (or a partly formylated derivative). This product was not purified but immediately hydrolysed and decarboxylated to the hydroxy-lactone (III) which was satisfactorily oxidised by chromium trioxide in acetic acid solution to the desired keto-lactone (IV). All yields are fairly good except for the final oxidation. The product was an oil, purified by distillation, and obtained in reasonable yield (65—75%), but proved to be a mixture from which (IV) was obtained as a crystalline solid (20—30%) leaving a liquid residue which has not been identified. Attempts have been made at each stage to determine optimum reaction conditions.

Our keto-lactone (IV) was a stable, colourless, crystalline, sharp-melting solid which could be distilled *in vacuo* (the Indian workers report a thick syrup decomposing during distillation under reduced pressure). Analysis indicated the formula $C_9H_{12}O_3$, the presence of a carbonyl function is shown by the ready formation of a mono-2 : 4-dinitrophenylhydrazone and monosemicarbazone (the latter differing in m. p. from that described by Paranjape *et al.*), and a lactone group is indicated by the behaviour with alkali. Values for the equivalent were consistently low, possibly owing to the formation of an acidic enediol (cf. ascorbic acid). The hydroxy-lactone (III) which cannot behave in this way gave satisfactory results. The spectrum of (IV) indicated the absence of any conjugated chromopheres.

Attempts to reduce (IV) to the known lactone of α-2-hydroxy*cyclo*hexylpropionic acid (which may be oxidised to the solid α-2-keto*cyclo*hexylpropionic acid) or to decarboxylate (IV) to 3-ethyl*cyclo*hex-2-enone were unsuccessful.

The method of synthesis is such that the only structural question remaining about (IV) is whether it is the γ- or the δ-lactone. The keto-group in the γ-lactone has one adjacent methylene group whilst in the δ-lactone it is flanked by two bridgehead positions. Although it has not been possible to prepare a benzylidene derivative in virtue of the reactive methylene group the presence of such a group has been indicated. The keto-lactone reacted readily with *N*-bromosuccinimide, or with bromine in acetic acid, to form a bromo-compound which was easily dehydrobrominated. The product has not been adequately characterised but was probably phenolic. Such a compound could result by bromination, dehydrobromination, lacto-enoic tautomerism, and dienone-phenol rearrangement, the last two reactions being catalysed by hydrogen bromide. Neither bromination nor subsequent dehydrobromination would occur very readily with the δ-lactone since this would involve bromination of tertiary hydrogen atoms and then the formation of double bonds at bridgehead positions in a bicyclic structure, the latter contrary to Bredt's rule (cf. Fawcett, *Chem. Reviews*, 1950, **47**, 219). (IV) was readily converted into a crystalline enol-acetate when heated with acetic anhydride and toluene-*p*-sulphonic acid (Bedoukian, *J. Amer. Chem. Soc.*, 1945, **67**, 1430). The γ-lactone should readily form an enol-acetate but the δ-lactone could only yield such a compound as an exception to Bredt's rule. It could be argued that under the acid conditions of this reaction the δ-lactone would undergo lacto-enoic tautomerism and then yield an enol-acetate [α-(2-acetoxy*cyclo*hexa-1 : 3-dienyl)propionic acid]. Such a compound would have the characteristic absorption of a conjugated diene shown to be absent from the compound actually obtained.

Thus, whilst it has not been possible to relate the keto-lactone to any known compound, indirect evidence suggests that it has the structure (IV).

Experimental

M. p.s are uncorrected. Absorption spectra were determined with a Unicam quartz spectrophotometer, ethanol being used as solvent.

Diethyl Methylmalonate.—Diethyl methylmalonate was prepared from malonic ester and methyl iodide. Unchanged malonic ester was removed by shaking the product for exactly one minute with (30%) sodium hydroxide solution.

Condensation of 3-*Bromo*cyclo*hexene with Diethyl Methylmalonate.*—3-Bromo*cyclo*hexene (Ziegler *et al.*, *loc. cit.*) was added to diethyl sodiomethylmalonate prepared from diethyl methylmalonate (44 g.) and sodium (6·5 g.) in ethanol (120 ml.). A fairly vigorous reaction ensued. After refluxing (30—60 minutes), alcohol was removed, water added, and the product extracted with ether. Diethyl *cyclo*hex-2-enylmethylmalonate (52 g., 73%) (I), b. p. 144—150°/12 mm., was obtained.

Condensation of 1 : 2-*Dibromo*cyclo*hexane with Diethyl Methylmalonate.*—1 : 2-Dibromo*cyclo*hexane (242 g.) (*Org. Synth.*, Coll. Vol. 1, 2nd Edn. p. 171) was added dropwise to diethyl methylmalonate (174 g.) in sodium ethoxide solution (from 48 g. of sodium and 800 ml. of ethanol) and the whole refluxed for 12 hours. This gave diethyl *cyclo*hex-2-enylmethylmalonate (163 g., 64%), b. p. 156—160°/16 mm., n_D^{17} 1·4670. (Lower yields were obtained after shorter or longer reflux periods.)

cyclo*Hex*-2-*enylmethylmalonic Acid.*—The ester (I) was hydrolysed (4N-ethanolic potassium hydroxide for 6 hours) to *cyclo*hex-2-enylmethylmalonic acid, obtained as a white microcrystalline solid (from benzene), m. p. 158° (decomp.) (lit., 137°) (Found: C, 60·8; H, 7·3. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%).

α-cyclo*Hex*-2-*enylpropionamide.*—The above malonic acid, heated at 165—170° for 30 minutes, gave α-*cyclo*hex-2-enylpropionic acid (91%), b. p. 140—147°/10 mm., $n_D^{18\cdot5}$ 1·4831. Treated with thionyl chloride and subsequently with ammonia this yielded α-*cyclo*hex-2-enylpropionamide, m. p. 129—134° (softens at 116°) (probably a mixture of racemates; Mousseron and Winternitz, *loc. cit.*, give m. p. 112—113°).

5-cyclo*Hex*-2-*enyl*-5-*methylbarbituric Acid.*—Urea (1·5 g.) in ethanol (12·5 ml.) was added to diethyl *cyclo*hex-2-enylmethylmalonate (6·4 g.) and sodium ethoxide solution [from sodium (0·58 g.) in ethanol (12·5 ml.)], the mixture was refluxed (7 hours), and hot water and concentrated hydrochloric acid were added. 5-cyclo*Hex*-2-*enyl*-5-*methylbarbituric acid* separated on cooling. Crystallised from ethanol, white needles, m. p. 208°, were obtained (Found: C, 59·8; H, 6·2; N, 12·6. $C_{11}H_{14}O_3N_2$ requires C, 59·5; H, 6·4; N, 12·6%).

cyclo*Hex*-1-*enylmethylmalonic Acid.*—Diethyl *cyclo*hex-1-enylmalonate was prepared and subsequently methylated to give diethyl *cyclo*hex-1-enylmethylmalonate and then hydrolysed, yielding *cyclo*hex-1-enylmethylmalonic acid according to the procedure of Kon and Speight (*loc. cit.*). The disubstituted malonic acid melted at 150—152° (decomp.) (lit., 155°) but this fell to 137—142° (decomp.) when the sample was mixed with the Δ^2-isomer obtained above. Decarboxylation was effected at 170° (15 minutes) and the residue converted into α-*cyclo*hex-1-enylpropionamide, m. p. 89—90° (Kandiah and Linstead, *J.*, 1929, 2139, cite 90°).

5-cyclo*Hex*-1-*enyl*-5-*methylbarbituric Acid.*—This acid was prepared from diethyl *cyclo*hex-1-enylmethylmalonate (1 g.) by the method described above, and crystallised from hot water as white needles, m. p. 190—194° (Found: C, 59·4; H, 6·0; N, 12·7. $C_{11}H_{14}O_3N_2$ requires C, 59·5; H, 6·4; N, 12·6%).

γ-*Lactone* (III) *of* α-(2 : 3-*Dihydroxy*cyclo*hexyl*)*propionic Acid.*—The diester (I) (63·5 g.), added to a mixture of 98—100% formic acid (265 g.) and 30% hydrogen peroxide (32·5 g.), was kept at 40—45° for 16 hours. (Similar yields were obtained at 40—45° for 4—24 hours and at 65—70° for 1—4 hours, but the longer heating was conveniently effected overnight.) Formic acid and unchanged diester (I) were removed by steam-distillation, leaving the partly formylated glycol [55 g., 77% (calc. as glycol)] (Found: equiv., 123·0. Calc. for free glycol: equiv., 144·2. Calc. for monoformyl derivative: equiv., 105·4), which was hydrolysed by 3N-methanolic potassium hydroxide (300 ml.) for 5 hours. Methyl alcohol was removed, and the residue mixed with hydrochloric acid and then evaporated to dryness. The resulting sticky solid, admixed with anhydrous sodium sulphate, was extracted with acetone in a Soxhlet extractor and distilled *in vacuo*, the γ-lactone (III) of α-(2 : 3-dihydroxy*cyclo*hexyl)propionic acid distilling at 154—156°/1 mm. (22 g., 66%) (Found: equiv., 173·2. Calc. for $C_{10}H_{14}O_3$: equiv., 172). This lactone solidified after several days at 0° but melted at room temperature;

attempts to crystallise it failed. Reaction with 3 : 5-dinitrobenzoyl chloride gave the 3 : 5-*dinitrobenzoate* as colourless platelets, m. p. 184—185°, after crystallisation from methanol (Found : C, 53·1; H, 4·5; N, 7·8. $C_{16}H_{16}O_8N_2$ requires C, 52·7; H, 4·4; N, 7·7%).

Lactone (IV) *of* α-(2-*Hydroxy*-3-*keto*cyclo*hexyl*)*propionic Acid.*—Attempts to oxidise the hydroxy-lactone (III) by the Oppenauer procedure were unsuccessful and the reaction was effected by chromium trioxide in acetic acid.

The hydroxy-lactone (21 g.) in acetic acid (85 ml.) was slowly stirred into a solution of chromium trioxide (9 g.) in water (9 ml.), diluted with acetic acid (85 ml.), at 10—15°. After 10 days at room temperature the reaction mixture was diluted (water) and continuously extracted (ether; 36 hours). The oily residue obtained on removal of the solvent was distilled. The distillate (b. p. 144—158°/1 mm.), dissolved in ether, slowly deposited crystals (m. p. 80—82°) at 0°. The yield of solid was 4·3—5·0 g. (20—24%) and of liquid 8·5—8·9 g. In some experiments, using 15% excess of chromium trioxide, these values were 6·5 g. (30%) and 7·5—8·0 g., respectively.

The liquid product (equiv., 145·5) gave a mixture of 2 : 4-dinitrophenylhydrazones from which no pure compounds were isolated.

The crystalline *lactone*, m. p. 86—87°, colourless prisms from ether or ethanol (Found : C, 64·3; H, 7·1%; equiv., 149—158. $C_9H_{12}O_3$ requires C, 64·3; H, 7·2%; equiv., 168·2), gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 168—170°, yellow plates from acetic acid (Found : N, 15·9. $C_{15}H_{16}O_6N_4$ requires N, 16·1%), and a *semicarbazone*, m. p. 195—197° (decomp.) (Paranjape *et al.*, give m. p. 150°), colourless prisms from ethanol (Found : C, 53·6; H, 6·5; N, 18·4. $C_{10}H_{15}O_3N_3$ requires C, 53·3; H, 6·7; N, 18·7%). In the early stages of this work before the keto-lactone was crystallised, carbonyl derivatives were obtained from the liquid distillate. These differed in m. p. from those already described : 2 : 4-*dinitrophenylhydrazone*, m. p. 206—210° (Found : C, 51·4; H, 4·6; N, 16·2. $C_{15}H_{16}O_6N_4$ requires C, 51·7; H, 4·6; N, 16·1%); *semicarbazone*, m. p. 202—203° (Found : C, 53·4; H, 6·6; N, 18·6%).

The thioacetal prepared from the keto-lactone (Wolfram and Karabinos, *J. Amer. Chem. Soc.*, 1944, **66**, 909) was refluxed with Raney nickel in ethanol but only traces of material could be obtained from the alcohol solution or from the nickel by extraction with acetone.

Reduction of the keto-lactone (2 g.) by Huang-Minlon's method (*J. Amer. Chem. Soc.*, 1946, **68**, 2457) gave a liquid (0·43 g.), b. p. 135—145°/8 mm. (bath-temp.), n_D^{20} 1·4760. This on oxidation (potassium permanganate) afforded an oil (0·27 g.) which could not be induced to crystallise.

Reduced by the Clemmensen procedure, the keto-lactone (2 g.) gave a liquid (0·47 g.), b. p. 140—150°/8 mm. (bath-temp.), which was oxidised (potassium permanganate) to a solid (0·21 g.) which could be purified only by repeated precipitation with acid from an alkaline solution, and then had m. p. 59—60° (Found : C, 68·3; H, 10·1. Calc. for $C_{17}H_{30}O_4$: C, 68·4; H, 10·6%); it has not been possible to suggest any structure for this substance.

Heated with aqueous hydrobromic–acetic acid (cf. Johnson, Peterson, and Schneider, *J. Amer. Chem. Soc.*, 1947, **69**, 74), the keto-lactone (1 g.) gave a crude solid (0·61 g.), of m. p. 105—125°, raised by extraction with light petroleum (b. p. 80—100°) and crystallisation of the extract from benzene–light petroleum (b. p. 80—100°) to m. p. 128—130° (Found : C, 65·9; H, 5·3%), which could not be identified.

When treated with ethanolic sulphuric acid according to the directions of Clemo, Cocker, and Hornsby (*loc. cit.*), the keto-lactone (1 g.) gave unchanged starting material (0·25 g.) and a liquid (0·037 g.), b. p. 140—155°/15 mm. (bath-temp.), which gave a small quantity of a yellow 2 : 4-dinitrophenylhydrazone accompanied by a dark red oil.

Unsuccessful attempts were made to prepare a benzylidene derivative by interaction of the keto-lactone with benzaldehyde in the presence of (*a*) 5N-sodium hydroxide, (*b*) sodium in toluene, and (*c*) piperidine acetate. The last reagent led to 2 : 6-dibenzylidene*cyclo*hexanone (33%) when refluxed for 24 hours with the required components.

Bromination of the Keto-lactone (IV).—(a) *Action of* N-*bromosuccinimide.* *N*-Bromosuccinimide (1·25 g.), heated under reflux with a solution of keto-lactone (1 g.) in carbon tetrachloride, produced, after a short induction period, a vigorous reaction with copious evolution of hydrogen bromide and separation of a brown oil. No succinimide crystallised on cooling. The solvent was removed by distillation under reduced pressure and the residue refluxed with pyridine (10 ml.) for 70 minutes. The solution, extracted with chloroform and washed with 6N-hydrochloric acid, afforded, on distillation, a liquid (0·61 g.), b. p. 120—140°/0·15 mm. (bath-temp.). This gave almost no 2 : 4-dinitrophenylhydrazone, was soluble in sodium hydroxide solution (blood-red colour) and sodium hydrogen carbonate solution (yellow colour), gave an indefinite

azo-dye test with aniline, and a dark brown precipitate with ferric chloride. The absorption spectrum of this liquid showed a maximum at 278 mμ (log ε 3·25) and a minimum at 253 mμ (log ε 3·10), probably due to a phenol (cf. Djerassi *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 990), and an inflexion at 220 mμ (log ε 3·60), probably due to a trace of unsaturated ketone.

(b) *Bromine in acetic acid.* Bromination with bromine in acetic acid at room temperature and subsequent dehydrobromination with collidine afforded an oil (0·55 g.) similar in properties to that obtained above.

Enol-acetate of the Keto-lactone (IV).—Toluene-*p*-sulphonic acid (0·5 g.), the keto-lactone (1 g.), and acetic anhydride (50 ml.) were refluxed for 1·5 hours. Acetic acid was removed by slow distillation through a short column for a further 2 hours, most of the acetic anhydride was then distilled off, and the remainder hydrolysed by shaking it with water (10 ml.). The product, extracted with chloroform, decolorised with charcoal, and further purified by dissolution in light petroleum (b. p. 80—100°) and removal of a small insoluble portion, was finally crystallised from light petroleum (b. p. 80—100°), giving the α-(3-*acetoxy*-2-*hydroxy*cyclo*hex*-3-*enyl*)*propionic lactone* (0·79 g., 63%), m. p. 124—126° (Found: C, 62·8; H, 6·3. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%).

We are indebted to the D.S.I.R. for a Maintenance Allowance to one of us (R. M. H.), to Mr. A. P. Tulloch for repeating the experiments of Kon and Speight, and to Mr. J. M. L. Cameron and Miss R. H. Kennaway for the microanalyses.

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249. *The Polarographic Reduction of Hydroxy- and Methoxy-anthraquinones.*

By L. A. WILES.

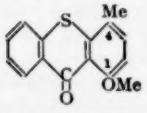
The behaviour at the dropping-mercury cathode of many hydroxyanthraquinones and of their methyl ethers has been studied.

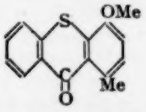
In strongly acid ethanol solution the methyl ethers are either reducible or non-reducible, and the division into these two well-marked classes is accounted for structurally. Under similar conditions hydroxyanthraquinones do not show such a clearly defined classification.

In alkaline solution all hydroxy- and methoxy-anthraquinones are reducible.

It is suggested that polarography can be used to give information on the configuration of some hydroxy- or methoxy-anthraquinones.

THE basic strength of methoxy-10-thioxanthones and methoxyxanthones was investigated by Smiles and his co-workers (Roberts and Smiles, *J.*, 1929, 863, 1322; Levi and Smiles, *J.*, 1931, 520; Roberts, Wiles, and Kent, *J.*, 1932, 1792), and was extended to methoxyanthraquinones by Roberts (*J.*, 1932, 1982). The basic strength of the parent ketone is increased greatly when a methoxy-group is substituted *ortho* to a carbonyl group; for instance, 1-methoxy-4-methyl-10-thioxanthone (I) is readily soluble in cold, concentrated hydrochloric acid, and forms a trihydrochloride at room temperature, whereas the isomeric 1-methyl-4-methoxy-10-thioxanthone (II) is much less soluble in hydrochloric acid and does not give an addition compound with hydrogen chloride under the same conditions. Similarly

(I) 

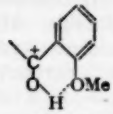


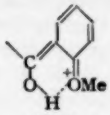
(II)

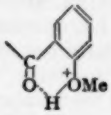
the formation of relatively stable salts by methoxyanthraquinones is confined to those compounds which have methoxyl in one or more of the α(1, 4, 5, or 8)-positions.

The theory of resonance would explain the stability of the salts of these methyl ethers by postulating the existence of various resonance forms which would confer stability on the system (cf. Sidgwick, *Ann. Reports*, 1933, **30**, 112; 1934, **31**, 40). The polar carbonyl group can form a salt by combining a proton with the oxygen atom, $>C=O \longrightarrow >C=\overset{+}{O}H$,

but the stability of such a compound is very small. Anthraquinone is, for example, a weak monoacid base, $K_b = 7 \times 10^{-23}$. With *o*-methoxy-ketones, however, resonance structures such as (III)—(V) would enhance the stability of the salts.


(III)


(IV)


(V)

Doubt has recently been cast on the extent of the contribution made by resonance effects in stabilising hydrogen bonds, and the bond may be largely electrostatic in nature ("Symposium on the Hydrogen Bond," Royal Institute of Chemistry Lectures, Monographs and Reports, 1950, No. 1. p. 18). If salts of *o*-methoxy-ketones have these hydrogen bonds it seemed likely that the reduction of a carbonyl group involved in the link might be hampered. It was therefore decided to examine polarographically the reduction of methoxyanthraquinines in acid and in alkaline media. For comparison an investigation of the corresponding hydroxyanthraquinones was made, since in these compounds the hydrogen of α-hydroxyl groups has an intramolecular bond with the carbonyl group.

Some previous work has been done on the polarographic reduction of compounds in which a hydrogen bond is linked with the reducible group to form a chelate ring. Scaramelli (*e.g., Atti R. Accad. Italia*, 1940, **1**, 764), studying the polarographic reduction of hydroxy- and alkoxy-substituted benzaldehydes and similar compounds, found that molecules in which intramolecular hydrogen bonding was to be expected were *more difficult* to reduce (*i.e.*, their reduction potentials were more negative) than molecules where the hydrogen bond was not possible. The reduction of nitrophenols has been examined by Astle and McConnell (*J. Amer. Chem. Soc.*, 1943, **65**, 35) and by Pearson (*Trans. Faraday Soc.*, 1948, **44**, 692). Although differing in their interpretation of the results, these workers agree that in acid solution the intramolecular hydrogen bond in *o*-nitrophenol allows the reduction of the nitro-group to proceed *more readily* than with *m*- and *p*-nitrophenol. The hydrogen bond in *o*-nitrophenol interferes with the resonance of the nitro-group, the oxygen atoms are no longer equivalent, and the compound loses stability. Similar results have been found with nitro-amidines (Runner, Kilpatrick, and Wagner, *J. Amer. Chem. Soc.*, 1947, **69**, 1406; Rabinowitz and Wagner, *ibid.*, 1951, **73**, 3030). Furman and Stone (*ibid.*, 1948, **70**, 3055) have examined the reduction potentials of a few hydroxyanthraquinones chiefly in alkaline solution with different buffers, so this aspect of the work has not been repeated.

Summary of Results.—The reduction potentials given in the following table are half-wave potentials ($-E_{\frac{1}{2}}$) in volts relative to the saturated calomel electrode. The solutions

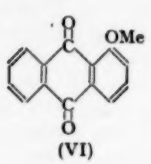
Position of substituents in anthraquinone (none)	Half-wave reduction potentials: Acid solution (pH 1·25) 0·18		Alkaline solution (pH 11·2) 0·75
	Hydroxyanthraquinone	Methoxyanthraquinone	
1-	0·21	0·12	0·73
2-	0·22	0·20	0·78
1 : 2-Di-	0·26	0·17	0·73
1 : 3-Di-	0·25	0·14	0·73
2 : 3-Di-	0·25	0·25	0·78
1 : 4-Di-	0·27	Not reducible	0·76
1 : 5-Di-	Not reducible	Not reducible	0·76
1 : 8-Di-	0·23	0·12	0·74
1 : 2 : 3-Tri-	0·27	0·14	0·73
1 : 2 : 4-Tri-	0·31	Not reducible	0·79
1 : 2 : 7-Tri-	0·27	0·17	0·73
1 : 2 : 5 : 8-Tetra-	0·30	Not reducible	0·75
1 : 4 : 5 : 8-Tetra-	Not reducible	Not reducible	0·79
2-Methyl-1 : 5 : 6 : 7-tetra-	—	Not reducible	0·74
2-Methyl-1 : 5-dihydroxy-6 : 7-di-	—	Not reducible	—

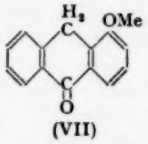
contained *ca.* 70% of ethanol, and the measured pH values are "apparent" values uncorrected for the non-aqueous solvent errors.

Methoxyanthraquinones which have methoxy-groups *ortho* to *both* carbonyl groups are not polarographically reducible in strongly acid solution. If one (or both) of the carbonyl groups has no *o*-methoxy-group then the compound is reducible. Hydroxyanthraquinones which have one of the carbonyl groups free from intramolecular hydrogen bonding are reducible in acid (*e.g.*, –OH at 1-, 2-, 2 : 3-, 1 : 2 : 7-). If both carbonyl groups have hydrogen bonds the compound may be reducible (*e.g.*, –OH at 1 : 4-, 1 : 2 : 4-, 1 : 2 : 5 : 8-) or it may not (*e.g.*, –OH at 1 : 5-, 1 : 4 : 5 : 8-). Methoxyanthraquinones which have methoxyl *ortho* to only one carbonyl group are more readily reducible than the corresponding hydroxyanthraquinones. Hydroxyanthraquinones are reduced with greater difficulty than anthraquinone.

Discussion of Results.—(a) *Methoxyanthraquinones.* The results suggest that the hydrogen-bridge structure postulated for salts of *o*-methoxy-ketones is probably correct. When both carbonyl groups are linked with methoxyl through hydrogen the salt may be resonance-stabilised and the non-reducibility of the compounds is to be expected. Alternatively, the absence of reduction may be attributed to the diminished proton-attracting power of the oxygen atom of the carbonyl groups owing to the attachment of the two bridge protons. If the resonance view is adopted then it seems that (IV) with its *o*-quinonoid form must play little part; if it did contribute to any extent all *o*-methoxyanthraquinones would be readily reducible. That the *o*-quinonoid resonance form is unlikely has also been inferred by Flett (*J.*, 1948, 1441) from the infra-red absorption spectrum of 1 : 4-dimethoxyanthraquinone.

Additional support for the hydrogen-bridge hypothesis is given by the work of Zahn and Koch (*Ber.*, 1938, **71**, 172), who showed that in the catalytic reduction of α-methoxyanthraquinones by hydrogen under pressure, *i.e.*, in the absence of acid, it is the carbonly group in the *peri*-position to the methoxy-group which is reduced, *e.g.*, 1-methoxyanthraquinone (VI) gives 1-methoxy-10-anthrone (VII).


(VI)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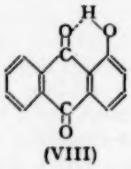
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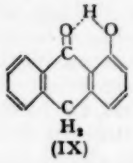
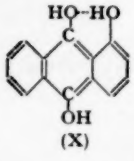
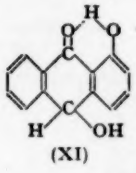
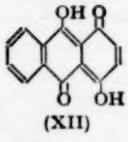

(IX)

(b) *Hydroxyanthraquinones.* The reduction of α-hydroxyanthraquinones by chemical reagents frequently leaves unaffected the carbonyl group linked with the hydrogen bond; *e.g.*, reduction of 1-hydroxyanthraquinone (VIII) by zinc and acetic acid gives 1-hydroxyanthrone (IX). Furman and Stone (*loc. cit.*) state that polarographic reduction of an


(X)


(XI)


(XII)

anthraquinone can produce the anthraquinol, so reduction of 1-hydroxyanthraquinone may occur as shown by (X). Alternatively, the reduction may leave the hydrogen bond intact and give an oxanthrone (XI). The results with hydroxyanthraquinones are not as simple as with methoxyanthraquinones and hydrogen bonding may be a complicating factor in the reduction of α-hydroxyanthraquinones.

1 : 4-Dihydroxyanthraquinone gives a well-defined reduction wave, but 1 : 5-dihydroxyanthraquinone is not reducible in acid solution. This implies a difference in the strengths

of the hydrogen bonds in these two compounds. Evidence of variation in the strength of hydrogen bonds in hydroxyanthraquinones has been adduced by Flett (*loc. cit.*), and he concludes that the hydrogen bonds in 1 : 4-dihydroxy- and 1 : 2 : 4-trihydroxy-anthraquinone are rather stronger than in the 1 : 5-dihydroxy-compound. On this evidence one would have expected that 1 : 4-dihydroxy- and 1 : 2 : 4-trihydroxy-anthraquinone would have been more difficult to reduce than 1 : 5-dihydroxyanthraquinone, whereas the reverse is the case. It is noteworthy that Green (*J.*, 1926, 1428; 1927, 2384) found chemical evidence for the behaviour of 1 : 4-dihydroxyanthraquinone as 1 : 10-dihydroxy-4 : 9-anthraquinone (XII) so the polarographic reduction may not proceed at carbonyl groups in the 9- or the 10-position.

Heyrovsky and Ilkovic (*Coll. Czech. Chem. Comm.*, 1935, **7**, 198) have shown that for reversible oxidation–reduction reactions a graph of the applied voltage (E) against log $i/(i_d - i)$ (where, at any point on the polarographic wave, i is the current produced by the applied voltage, and i_d is the diffusion current) gives, at 25°, a straight line of slope $0{\cdot}059/n$, where n is the number of electrons involved in the reaction. Some hydroxy- and methoxy-anthraquinones were examined in this way in acid and in alkaline solution. In general, the graphs show that the reductions are not reversible processes. A possible exception is 1-methoxyanthraquinone in acid solution, for which a straight line of slope 0·033 corresponds approximately to a 2-electron reduction.

Suggested Application of the Foregoing Results.—The differences in the ease of reduction of methoxy- and hydroxy-anthraquinones may prove useful in confirming the structure of some anthraquinones. The hydroxy-compounds and their methyl ethers frequently occur in Nature, and their isolation is often difficult and in poor yield. The use of the polarograph is attractive as it requires extremely small amounts of pure material. The following illustrates a likely application of the method.

1 : 2 : 3 : 5- *and* 1 : 2 : 3 : 7-*Tetrahydroxyanthraquinone.* Condensation of gallic acid and *m*-hydroxybenzoic acid gives two isomeric tetrahydroxy-compounds, one insoluble and the other difficultly soluble in benzene. These were first isolated by Noah (*Ber.*, 1886, **19**, 2337) but he was not able to distinguish them. The assignment to them of definite configurations (*e.g.*, Thorpe, " Dictionary of Applied Chemistry," 4th edtn., **1**, 226; Heilbron, " Dictionary of Organic Compounds," 1st edn., Vol. III, p. 710) is not based on published evidence. Briggs (*J.*, 1948, 990) has tentatively advanced reasons for believing that the 1 : 2 : 3 : 5-isomer is the one more soluble in benzene, and it is likely that its tetramethyl ether will not be reducible polarographically in acid solution whereas the corresponding 1 : 2 : 3 : 7-tetramethyl ether should be. This matter is being investigated.

Experimental

A Cambridge Instrument Co. polarograph giving photographic recording of the current–voltage curves was used. The instrument was operated so that the rate of change of voltage was the slowest available, *viz.*, 1·0 volt in 80 seconds. The form of the reduction waves was sometimes improved by using the expanded scale technique (Werthessen and Baker, *Endocrinology*, 1945, **36**, 351) in which the normal 6-volt input to the potentiometer was reduced to 2 volts. No correction of the half-wave potentials for the voltage drop in the circuit was necessary as the values were very small and did not exceed the accuracy with which the potentials could be read from the polarograms. The dropping-mercury electrode had the following characteristics: the drop time (t) on open circuit into 0·1M-potassium chloride solution was 3·35 seconds, the weight of mercury dropping per second (m) was 1·649 mg., and $m^{2/3}t^{1/6}$ was 1·71.

The acid solvent contained *ca.* 70% of ethanol. It was saturated with potassium chloride as the supporting electrolyte, and concentrated hydrochloric acid was added to give a strongly acid solution the pH of which was measured by a Marconi meter. The alkaline solvent also contained *ca.* 70% of ethanol. In order that it should be adequately buffered it was made 0·2M with both boric acid and sodium hydroxide, and it was also saturated with potassium chloride. The measured pH was 11·2 and that estimated by British Drug Houses " Narrow Range " Indicator papers was 8·5—8·8. Both acid and alkaline solvents were polarographed to ensure that they contained no reducible substances likely to cause interference with the reduction waves. Where possible the anthraquinone solutions were 10^{-3}M, but solubility sometimes

limited the concentrations to smaller values, and a saturated solution of the anthraquinone was then used.

The cell containing the solution under examination, the dropping-mercury electrode, and the saturated calomel electrode were immersed in a water-bath regulated at 25° ± 0·1°. Before a photographic record was made the anthraquinone solutions were de-oxygenated by bubbling oxygen-free nitrogen through them for about 30 minutes.

The hydroxyanthraquinones were commercial samples and were purified by crystallization from ethanol or acetic acid, or by sublimation. The methoxyanthraquinones were prepared from the hydroxy-compounds by the use of methyl sulphate and alkali. The resistance of hydroxyl at the 1-, 4-, 5-, or 8-positions to methylation was frequently encountered and it was generally best to use the method outlined below.

The following two compounds are new.

1 : 2 : 4-*Trimethoxyanthraquinone.* Potassium hydroxide (3 mols.) was dissolved in methyl alcohol, 1 : 2 : 4-trihydroxyanthraquinone (1 mol.) was added, and the solvent evaporated. The dry potassium salt was intimately mixed with anhydrous potassium carbonate (10 mols.) and transferred to a large boiling-tube. Methyl sulphate (10 mols.), dissolved in an equal volume of acetone, was added so that the solid was well saturated with the liquid, and the acetone then evaporated. The mixture was heated at 180° for 7 hours under reflux. After extraction with 10% sodium hydroxide solution the *trimethoxy*-compound crystallized from ethanol in fine yellow needles, m. p. 168° (corr.) (Found: C, 68·5; H, 4·7; OMe, 30·0. $C_{17}H_{14}O_5$ requires C, 68·5; H, 4·7; OMe, 31·2%).

1 : 2 : 5 : 8-*Tetramethoxyanthraquinone.* This *compound*, prepared from the tetrahydroxy-compound by the above method, crystallized from ethanol in golden-yellow needles, m. p. 202° (corr.) (Found: C, 65·6; H, 5·0; OMe, 36·7. $C_{18}H_{16}O_6$ requires C, 65·9; H, 4·9; OMe, 37·8%).

The following anthraquinones had m. p.s (corr.) which differed from previously recorded values (lit. values in parentheses): 1 : 2 : 3-trihydroxy-, 316° (310°, 312—313°, 313—314°); 1 : 4-dimethoxy-, 172° (143°, 170—171°).

M. p.s (corr.) for the following anthraquinones are also recorded, as literature values are inconsistent: 1-hydroxy-, 194—195° (190°, 191°, 193°, 190—193°, 200—201°); 2-hydroxy-, 312° (302°, 305°, 306°, 302—306°, 314°); 1 : 4-dihydroxy-, 194° (193°, 194°, 197—198°, 200—202°),* bronze plates from acetic acid; 1 : 2 : 4-trihydroxy-, 257° (253°, 253—254°, 255—257°, 259°); 1 : 3-dimethoxy-, 164° (151—153°, 155°, 164—165°); 1 : 5-dimethoxy-, 237° (234—236°, 236°, 238—240°, 241°).

The author acknowledges his indebtedness to Emeritus Professor S. Smiles, F.R.S., who suggested the work, and to Professor E. C. Baughan for his advice. Thanks are due to Imperial Chemical Industries Limited, British Celanese Ltd., and L. B. Holliday & Co., Ltd., for gifts of chemicals, and to Dr. L. H. Briggs for specimens of 1 : 5 : 6 : 7-tetramethoxy-2-methylanthraquinone (areolatin tetramethyl ether) and 1 : 5-dihydroxy-6 : 7-dimethoxy-2-methylanthraquinone (areolatin dimethyl ether). Mr. D. A. Swann and Mr. K. B. Tucker kindly assisted with the preparative work. Microanalyses are by Drs. Weiler and Strauss, Oxford.

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[*Received, October 3rd*, 1951.]

* According to Lindpainter (*Mikrochemie*, 1937, **27**, 27) this compound has two enantiotropic forms, one orange, m. p. 195°, and the other dark red, m. p. 201°.

250. *The Preparation and Properties of Some Hydrocarbons with Recurrent Groups.*

By S. F. Birch, V. E. Gripp, D. T. McAllan, and W. S. Nathan.

Six hydrocarbons of high molecular weight, with methyl, tetramethylene, and pentamethylene substituent groups attached to a paraffin chain, have been prepared from the corresponding long-chain dicarboxylic esters *via* the glycols and dibromides. The esters were obtained by anodic oxidation of the acid esters of ββ-disubstituted glutaric acids. Physical properties of the hydrocarbons are described.

Attempts to correlate the physical properties of hydrocarbons with structure have been considerably hampered by lack of reliable data for the higher and more complex members. We have prepared a series of hydrocarbons in which a recurrent group occurs as in certain types of polymers. Our recurrent groups were (I), (II), and (III).

$$\underset{\text{(I)}}{-CH_2\cdot CMe_2\cdot CH_2-} \qquad \underset{\text{(II)}}{[CH_2]_5{>}C(CH_2-)_2} \qquad \underset{\text{(III)}}{[CH_2]_4{>}C(CH_2-)_2}$$

Hydrocarbons based on (II) and (III) form a new series.

We prepared six hydrocarbons—three containing two and three containing four of these repeating units. The method of preparation was anodic oxidation of the sodium salt of the acid ester of a dibasic organic acid :

$$2RO_2C\cdot[CH_2]_n\cdot CO_2H \longrightarrow RO_2C\cdot[CH_2]_{2n}\cdot CO_2R + 2CO_2 + H_2$$

followed by reduction of the diesters to the glycols, conversion of the latter into dibromides, and finally reduction to the hydrocarbons. The yields were 50—70% overall from the esters.

There are several practical limitations to building up a molecule of relatively high molecular weight by successive electrolyses. At each succeeding electrolysis, the yield decreases owing to increased formation of by-products. These are difficult to separate when they boil outside the range of normal distillation, but might be removed by use of, *e.g.*, selective solvents. Another difficulty is due to the decreasing solubility of the intermediate derivatives.

Our starting materials were ββ-dimethylglutaric, *cyclo*hexane- and *cyclo*pentane-1 : 1-diacetic acids. With acetic anhydride these gave the anhydrides from which the methyl hydrogen esters were obtained by treatment with sodium methoxide solution. In the preliminary work, ethyl esters were employed for electrolysis with absolute methanol as electrolyte but the exchange of methyl and ethyl groups between ester and electrolyte caused difficulty. The exclusive use of methyl esters obviated this. A further modification was the replacement of pure methanol as electrolyte by a mixture of equal parts of methanol and light petroleum. The resulting increase in solubility of esters in the electrolyte enabled more concentrated solutions to be electrolysed with consequent decrease in undesirable reaction products. Also, cooling of the reaction vessel became unnecessary since the temperature was controlled at the reflux temperature (50—54°). Electrolysis of the above three methyl hydrogen esters yielded the substituted dimethyl suberates. Conversion of these into the methyl hydrogen esters, followed by electrolysis of the sodium salts yielded the dimethyl dodecane-1 : 12-dicarboxylates.

The six dimethyl esters were reduced to the glycols by lithium aluminium hydride (Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 1197), then converted into the dibromide by anhydrous hydrogen bromide, and reduced with zinc dust and refluxing glacial acetic acid to the hydrocarbons, the physical properties of which are tabulated below. The only recorded reference to these hydrocarbons is that Whitmore and Carney (*ibid.*, 1941, **63**, 2633) isolated a small amount of impure 3 : 3 : 6 : 6-tetramethyloctane after reaction of sodium with 1-chloro-2 : 2-dimethylbutane.

Experimental

Analyses were carried out by Drs. Weiler and Strauss, Oxford.

General Method of Electrolysis.—A 2-l. wide-mouthed bottle was fitted with a cork supporting a reflux condenser, a thermometer, and a glass rack as an electrode support. The electrodes consisted of a sheet platinum anode (4 × 6 cm.) with two sheet iron cathodes of similar dimensions spaced 5 mm. away on either side, all held firmly in the glass rack. The respective electrode leads were of stout platinum and iron wire spot-welded to the electrodes and sealed into glass tubes passing through the cork. The current was taken from the 100-v D.C. supply through a rheostat and ammeter.

Electrolysis of each acid ester was carried out in a mixture of methanol and light petroleum (b. p. 70—90°) to which a small amount (3 g.) of metallic sodium * had been added. The reaction proceeded under reflux at a current of 2—3 amp. until a 25% excess over the theoretical amount of electricity had been used.

Ref.	Hydrocarbon	B. p.°/mm.	M. p. Found [b]	M. p. Calc.[a]	d^{20}	d^{25}	Purity, mol.% [b]
A	3 : 3 : 6 : 6-Tetramethyloctane	189·7°/760 130°/140	−73·59°	−73·28°	0·7617	0·7570	99·0
B	3 : 3 : 6 : 6 : 9 : 9 : 12 : 12-Octamethyltetradecane	191·3°/23·3	Glass	—	0·8061	0·8030	—
C	3 : 3-6 : 6-Di(pentamethylene)-octane	218·7°/20·5	+ 7·06	+ 7·40	0·9025	0·8992	99·0
D	3 : 3-6 : 6-9 : 9-12 : 12-Tetra-(pentamethylene)tetradecane	—	+70—71	—	—	—	—
E	3 : 3-6 : 6-Di(tetramethylene)-octane	105°/1·5	−15·66	−14·83	0·8808	0·8775	97·5
F	3 : 3-6 : 6-9 : 9-12 : 12-Tetra-(tetramethylene)tetradecane	—	+65	—	—	—	—

* Calc. for zero impurity. [b] Freezing points were determined by the method of Mair, Glasgow, and Rossini (*J. Res. Nat. Bur. Stand.*, 1941, **26**, 591) and purity was estimated by the method of Glasgow, Streiff, and Rossini (*ibid.*, 1945, **35**, 355).

Refractive indices at various wave-lengths (Å).

Hydrocarbon ref.	Hydrogen (6562) 20°	Hydrogen (6562) 25°	Sodium (5893) 20°	Sodium (5893) 25°	Mercury (5460) 20°	Mercury (5460) 25°	Hydrogen (4861) 20°	Hydrogen (4861) 25°	Mercury (4358) 20°	Mercury (4358) 25°	Kinematic viscosity, centistokes/deg. 20°	37·8°	98·9°
A	1·4242	1·4222	1·4265	1·4244	1·4284	1·4263	1·4316	1·4296	1·4360	1·4338	2·15	1·615	0·795
B	1·4475	1·4457	1·4498	1·4481	1·4519	1·4501	1·4554	1·4534	1·4598	1·4581	60·37	22·51	3·66
C	1·4868	1·4852	1·4894	1·4875	1·4914	1·4897	1·4954	1·4935	1·5002	1·4985	51·82	20·61	3·57
E	1·4745	1·4729	1·4768	1·4755	1·4789	1·4778	1·4827	1·4810	1·4873	1·4868	—	—	—

Methyl Hydrogen ββ-Dimethylglutarate.—ββ-Dimethylglutaric acid (800 g.) was refluxed for 1 hour with acetic anhydride (430 g.). The excess of the latter, together with the acetic acid formed, was removed by distillation and the residual ββ-dimethylglutaric anhydride distilled at atmospheric pressure. The anhydride, m. p. 121°, was obtained in theoretical yield and converted into the acid ester by slowly adding the finely-ground material (710 g.) to a well-stirred solution of sodium methoxide (116 g. of sodium in 3 l. of methanol) at 0°. The mixture was allowed to warm slowly to room temperature and, after a further hour, gently refluxed for 1 hour. After addition of water (3 l.) the methanol was removed on the water-bath and the acid ester liberated by the addition of excess of hydrochloric acid. The crude product was dried by distillation with benzene, the last traces of which were removed under reduced pressure. The acid ester (850 g., 100%) was used for the next stage without further treatment.

Dimethyl ββββ′β′-Tetramethylsuberate.—Methyl hydrogen ββ-dimethylglutarate (104 g.) was dissolved in 1 : 1 mixture (1·3 l.) of methanol and light petroleum to which metallic sodium (3 g.) had been added. Electrolysis was allowed to proceed at reflux temperature (54°) until a 25% theoretical excess of electricity had been passed. The product was filtered from deposited sodium carbonate and, after evaporation of the filtrate on the water bath, the residue was dissolved in benzene (100 ml.). After being washed with 5N-hydrochloric acid (100 ml.), the benzene solutions from eight such electrolyses were combined and evaporated and the residue

* The use of potassium in recent work has proved advantageous.

fractionated at reduced pressure through a short column. Dimethyl ββββ′β′-tetramethylsuberate distilled at 143·5°/10 mm. and 292°/760 mm., with n_D^{20} 1·4435, in 75% yield (Walker and Wood, *J.*, 1906, **89**, 598, obtained a 40% yield) (Found: C, 65·1; H, 10·1. Calc. for $C_{14}H_{26}O_4$: C, 65·1; H, 10·4%).

The free acid, obtained by hydrolysis with alcoholic potassium hydroxide and crystallised from methanol, melted at 169·5° (Walker and Wood gave 164—165°) (Found: C, 62·8; H, 9·6. Calc. for $C_{12}H_{20}O_4$: C, 62·6; H, 9·6%).

3 : 3 : 6 : 6-*Tetramethyloctane*-1 : 8-*diol*.—Lithium aluminium hydride (38 g.; 1 mole) was dissolved in dry ether (1 l.) in a 3-l. three-necked round-bottomed flask fitted with a sealed Hershberg stirrer, dropping funnel, and an efficient reflux condenser (calcium chloride tube). A solution of dimethyl tetramethylsuberate (194 g., 0·75 mole) in ether (500 ml.) was added to the vigorously stirred solution as fast as the exothermic reaction would allow. Stirring was continued for an hour after the addition was complete and the excess of hydride destroyed by careful addition of water. Hydrolysis was carried out with 10% sulphuric acid (1500 ml.) and, after separation of the ether layer, the aqueous layer was thoroughly extracted with ether. The combined ethereal layers were washed with sodium hydrogen carbonate solution, dried, and filtered, and the ether was removed on the water-bath. The residue distilled at 156—158°/3 mm. and the distillate crystallised at low temperature from ether, yielding the pure *glycol* (112 g., 74·5%), m. p. 48—49° (Found: C, 71·4; H, 13·1. $C_{12}H_{26}O_2$ requires C, 71·2; H, 13·0%).

The material recovered from the mother-liquors was re-treated with lithium aluminium hydride, the final yield of **3 : 3 : 6 : 6-*tetramethyloctane*-1 : 8-*diol*** being 92·5% (140 g.). The ***phenylurethane*** derivative, crystallised from light petroleum, melted at 101·5—102·5° (Found: C, 71·0; H, 7·9; N, 6·4. $C_{26}H_{36}O_4N_2$ requires C, 70·9; H, 8·2; N, 6·4%). The **3 : 5-*dinitrobenzoate*** melted at 134—135° (Found: C, 53·3; H, 5·4; N, 9·3. $C_{26}H_{30}O_{12}N_4$ requires C, 52·9; H, 5·1; N, 9·5%).

1 : 8-*Dibromo*-3 : 3 : 6 : 6-*tetramethyloctane*.—The glycol (135 g.) was treated at 120° with hydrogen bromide till absorption was complete and the product extracted with light petroleum. After successive washing with water, concentrated sulphuric acid, and sodium hydrogen carbonate solution, the extract was dried ($CaCl_2$) and filtered and the solvent removed. The crude product (187 g., 85%) was purified by crystallisation from light petroleum, to yield **1 : 8-*dibromo*-3 : 3 : 6 : 6-*tetramethyloctane***, m. p. 21·5° (Found: C, 44·5; H, 6·6; Br, 48·8. $C_{12}H_{24}Br_2$ requies C, 43·9; H, 7·4; Br, 48·7%).

3 : 3 : 6 : 6-*Tetramethyloctane*.—The dibromide (164 g., 0·5 mole) and glacial acetic acid (1·5 l.) were placed in a 3-l. flask fitted with a Hershberg stirrer and a reflux condenser. Zinc dust (500 g.) was added to the vigorously stirred solution which was refluxed for 48 hours with the addition of more zinc dust (100 g.) after 24 hours. The solution was diluted with an equal volume of water and steam-distilled, to yield the crude hydrocarbon which was dissolved in light petroleum and washed with concentrated sulphuric acid, 10% sodium hydroxide solution, and water. After drying (K_2CO_3), the solvent was removed, and the **3 : 3 : 6 : 6-tetramethyloctane** (70 g., 82·5%) distilled as a colourless oil at 74°/12 mm. (Found: C, 85·0; H, 15·2. Calc. for $C_{12}H_{26}$: C, 84·6; H, 15·4%).

***Methyl Hydrogen* ββββ′β′-*Tetramethylsuberate*.**—Dimethyl tetramethylsuberate (378 g.) was refluxed with an equimolecular quantity of acetic acid (88 ml.) and concentrated hydrochloric acid (20 ml.). Methyl acetate was removed as formed through a short column until 0·33 equiv. had distilled. Further reaction was stopped by adding benzene (200 ml.), and the water removed by distillation with the benzene. Acetic acid was then distilled off and the residue fractionated at reduced pressure, to yield unchanged dimethyl ester, b. p. 142—146°/11 mm., n_D^{20} 1·4437, and the required acid methyl ester, b. p. 183°/10 mm., n_D^{20} 1·4530, m. p. 27°. The residue of tetramethylsuberic acid was combined with the unchanged dimethyl ester and, after addition of the calculated quantity of acetic and hydrochloric acids, the procedure was repeated several times. The final yield of acid ester was 83% (297 g.) with only a small residue (21 g.) of neutral ester and acid.

Dimethyl* 2 : 2 : 5 : 5 : 8 : 8 : 11 : 11-*Octamethyldodecane*-1 : 12-*dicarboxylate*.**—The methyl hydrogen ββββ′β′-tetramethylsuberate (344 g.) was electrolysed under the conditions previously described. After removal of solvent, the residue was dissolved in benzene and washed with sodium hydrogen carbonate solution. The solution was dried by distilling the benzene, and the residue distilled through a small column to an overhead temperature of 162°. The residual oil was finally fractionated at reduced pressure, to give the ***dodecanedicarboxylate (205 g., 75%), b. p. 137°/0·5 mm., n_D^{20} 1·4560 (Found: C, 72·3; H, 11·6. $C_{24}H_{44}O_4$ requires C, 72·8; H, 11·7%). The free ***acid***, liberated from the potassium salt after saponification, crystallised from

methanol as a white microcrystalline powder, m. p. 135° (Found: C, 71·2; H, 11·4. $C_{22}H_{42}O_4$ requires C, 71·3; H, 11·4%).

3 : 3 : 6 : 6 : 9 : 9 : 12 : 12-*Octamethyltetradecane*-1 : 14-*diol*.—The above ester (279 g., 0·7 mol.) was reduced with lithium aluminium hydride (38 g.; 1 mol.) in ether (3 l.). The crude product (235 g., 98%), on crystallisation from ether, yielded the *diol*, m. p. 82—83° (Found: C, 77·2; H, 13·3. $C_{22}H_{46}O_2$ requires C, 77·2; H, 13·5%). The *phenylurethane* derivative crystallised from light petroleum as fine needles, m. p. 112—113° (Found: C, 74·1; H, 9·6; N, 5·2. $C_{35}H_{56}O_4N_2$ requires C, 74·4; H, 9·7; N, 4·8%).

1 : 14-*Dibromo*-3 : 3 : 6 : 6 : 9 : 9 : 12 : 12-*octamethyltetradecane*.—The glycol (230 g.) was esterified as above. The crude dibromide (315 g.) was obtained in theoretical yield. After repeated crystallisations from light petroleum at low temperature, the 1 : 14-*dibromo*-3 : 3 : 6 : 6 : 9 : 9 : 12 : 12-*octamethyltetradecane* (210 g.) melted at 42·0—42·5° (Found: C, 56·5; H, 9·3; Br, 34·3. $C_{22}H_{44}Br_2$ requires C, 56·4; H, 9·5; Br, 34·1%).

3 : 3 : 6 : 6 : 9 : 9 : 12 : 12-*Octamethyltetradecane*.—The dibromide (234 g.) was stirred with zinc dust and refluxing glacial acetic acid for 48 hours. After dilution with water, the solution was extracted with light petroleum and the extract washed with concentrated sulphuric acid, 10% sodium hydroxide, and water, before drying ($CaCl_2$). The solvent was removed and 3 : 3 : 6 : 6 : 9 : 9 : 12 : 12-*octamethyltetradecane* (132 g., 85%) distilled as a viscous oil at 115°/0·4 mm. (Found: C, 85·2; H, 14·9. $C_{22}H_{46}$ requires C, 85·1; H, 14·9%).

Methyl Hydrogen cyclo*Pentane*-1 : 1-*diacetate*.—*cyclo*Pentane-1 : 1-diacetic acid was refluxed for 3 hours with excess of acetic anhydride; after distillation of acetic acid and acetic anhydride, the residual *cyclo*pentane-1 : 1-diacetic anhydride was obtained as a brown solid. Crystallisation from light petroleum gave fine colourless needles, m. p. 68°. The anhydride (568 g.) was added with shaking to a solution of sodium (78 g.) in methanol (3 l.) which was cooled in an ice-bath till dissolution was complete. The solution was allowed to warm overnight to room temperature and, after 2 hours' refluxing, water (3 l.) was added. Methanol was removed by distillation and the acid ester liberated by the addition of hydrochloric acid, separated, and dried by distillation with benzene. On removal of the benzene the acid ester was obtained in theoretical yield (661 g.).

Dimethyl 2 : 2-5 : 5-*Di*(*tetramethylene*)*hexane*-1 : 6-*dicarboxylate*.—Methyl hydrogen *cyclo*pentane-1 : 1-diacetate (661 g.) was electrolysed as previously described and worked up in the normal way. The product was distilled to 122°/12·5 mm. and the residue (330 g.) distilled in the range 105—110°/0·04 mm. Fractionation in a 16-plate spinning-band column (Birch, Gripp, and Nathan, *J. Soc. Chem. Ind.*, 1947, **66**, 33) yielded a fraction (170 g.), b. p. 139°/0·5 mm., n_D^{20} 1·4793, which proved to be the required diester. It was dissolved in ether and washed with sodium hydrogen carbonate solution to remove traces of *cyclo*pentane-1 : 1-diacetic acid. The *dimethyl* ester was finally refractionated and obtained as a colourless oil, n_D^{20} 1·4790, d^{20} 1·043 (Found: C, 69·7; H, 9·8. $C_{18}H_{30}O_4$ requires C, 69·6; H, 9·8%). A small quantity of the ester was hydrolysed to yield the free *acid* which crystallised from acetone as rhombic crystals, m. p. 170° (Found: C, 68·2; H, 9·0. $C_{16}H_{26}O_4$ requires C, 68·1; H, 9·3%).

3 : 3-6 : 6-*Di*(*tetramethylene*)*octane*-1 : 8-*diol*.—The above ester (31 g., 0·1 mol.) was reduced with lithium aluminium hydride to the *glycol* (22 g., 87%) which crystallised from ether as a microcrystalline powder, m. p. 110—111° (Found: C, 75·9; H, 11·9. $C_{16}H_{30}O_2$ requires C, 75·5; H, 11·9%).

1 : 8-*Dibromo*-3 : 3-6 : 6-*di*(*tetramethylene*)*octane*.—This *dibromide* (25 g., 80%), obtained from the above glycol (21 g.) and crystallised from light petroleum at low temperature, had m. p. 59—60° (Found: C, 51·2; H, 7·5; Br, 41·7. $C_{16}H_{28}Br_2$ requires C, 50·5; H, 7·4; Br, 42·0%).

3 : 3-6 : 6-*Di*(*tetramethylene*)*octane*.—The dibromide (22 g.) was reduced with zinc dust and refluxing glacial acetic acid and the resultant hydrocarbon treated as described previously. The 3 : 3-6 : 6-*di*(*tetramethylene*)*octane* (9·5 g., 75%) distilled at 105°/1·5 mm. as a colourless oil (Found: C, 86·7; H, 13·4. $C_{16}H_{30}$ requires C, 86·4; H, 13·6%).

Methyl Hydrogen 2 : 2-5 : 5-*Di*(*tetramethylene*)*hexane*-1 : 6-*dicarboxylate*.—Dimethyl 2 : 2-5 : 5-di(tetramethylene)hexane-1 : 6-dicarboxylate (157 g.) was dissolved at 5° in a solution of potassium hydroxide (28·5 g.) in methanol (450 ml.). The mixture was held at this temperature for 36 hours in a refrigerator, allowed to attain room temperature for 12 hours, and finally refluxed for 3 hours. After addition of water (500 ml.), methanol was distilled off and unchanged ester separated by extraction of the aqueous solution with light petroleum. The aqueous layer was then acidified with hydrochloric acid and extracted with warm light petroleum, and the extract cooled overnight at 5°. The required acid ester (83 g.) was obtained

by removal of the solvent. The recovered acid was dissolved in methanol (100 ml.) and esterified, with sulphuric acid (10 ml.) as catalyst. The total bulk of recovered diester was then reprocessed and the bulked crude acid ester was fractionated in a 16-plate spinning-band column, to give methyl hydrogen 2 : 2-5 : 5-di(tetramethylene)hexane-1 : 6-dicarboxylate (108·5 g.), b. p. 150°/0·25 mm., n_D^{20} 1·4891.

Dimethyl 2 : 2-5 : 5-8 : 8-11 : 11-*Tetra(tetramethylene)dodecane*-1 : 12-*dicarboxylate*.—The acid ester (108 g.) was electrolysed, 50% excess current being used, and the product processed in the usual way. On fractionation in a spinning-band column, a high-boiling fraction was obtained at 172—180°/0·02 mm., which slowly crystallised. This solid (24·5 g.) was resolved into three components by crystallisation from dilute methanol at low temperature. They were a viscous oil, a trace (0·5 g.) of a microcrystalline powder, m. p. 145°, and *dimethyl* 2 : 2-5 : 5-8 : 8-11 : 11-*tetra(tetramethylene)dodecane*-1 : 12-*dicarboxylate* (18 g.), colourless needles, m. p. 56° (Found : 76·4; H, 10·8. $C_{32}H_{54}O_4$ requires C, 76·6; H, 10·8%). A small quantity of the free *acid* was obtained which crystallised from acetone as colourless needles, m. p. 175° (Found : C, 75·4; H, 10·2. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

3 : 3-6 : 6-9 : 9-12 : 12-*Tetra(tetramethylene)tetradecane*-1 : 14-*diol*.—The ester (15 g., 0·03 mol.) was reduced by lithium aluminium hydride (5 g.) in ether (300 ml.), the ester being dissolved from the thimble of a Soxhlet extractor fitted between the flask and reflux condenser by the refluxing solvent. The *diol* (13 g.) crystallised from ether as a microcrystalline powder, m. p. 110—111° (Found : C, 80·4; H, 12·1. $C_{30}H_{54}O_2$ requires C, 80·65; H, 12·2%).

1 : 14-*Dibromo*-3 : 3-6 : 6-9 : 9-12 : 12-*tetra(tetramethylene)tetradecane*.—The diol (12 g.) yielded the *dibromide* (14·5 g., 94%) which, crystallised from light petroleum at low temperature, had m. p. 71—72° (Found : C, 62·8; H, 9·4; Br, 27·6. $C_{30}H_{52}Br_2$ requires C, 62·9; H, 9·2; Br, 27·9%).

3 : 3-6 : 6-9 : 9-12 : 12-*Tetra(tetramethylene)tetradecane*.—The dibromide (13 g.) was reduced by zinc dust and refluxing glacial acetic acid and the product isolated as before. The *hydrocarbon* (6·5 g., 70%) crystallised from methylene chloride at low temperature as colourless needles, m. p. 65° (Found : C, 87·0; H, 12·9. $C_{30}H_{54}$ requires C, 86·9; H, 13·1%).

Methyl Hydrogen cyclo*Hexane*-1 : 1-*diacetate*.—*cyclo*Hexane-1 : 1-diacetic anhydride was prepared in 85% yield from *cyclo*hexanediacetic acid as described for *cyclo*pentanediacetic anhydride. The finely powdered anhydride, m. p. 69°, was slowly added to a stirred solution of sodium (95 g.) in methanol (3 l.) at 0°. When dissolution was complete the mixture was allowed to warm to room temperature and then refluxed for 2 hours. Excess of methanol was distilled off, the residue dissolved in water (3 l.), and the acid ester liberated with a slight excess of hydrochloric acid. It was extracted with benzene and dried by distillation of the benzene. The methyl hydrogen *cyclo*hexane-1 : 1-diacetate was obtained in theoretical yield (879 g.).

Dimethyl 2 : 2-5 : 5-*Di(pentamethylene)hexane*-1 : 6-*dicarboxylate*.—The acid ester described above was electrolysed in batches (145 g.) in the usual way. Distillation of the crude product to 200°/16 mm. removed the by-products and the residue was fractionated in a spinning-band column. The *dimethyl* ester, b. p. 148—152°/0·3 mm., crystallised from acetone at low temperature as large prisms (265 g.), m. p. 40·5°, in 38% yield (Found : C, 71·2; H, 9·9. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·1%). The free *acid* crystallised from acetone as small colourless prisms, m. p. 194° (Found : C, 69·4; H, 9·6. $C_{18}H_{30}O_4$ requires C, 69·7; H, 9·7%).

3 : 3-6 : 6-*Di(pentamethylene)octane*-1 : 8-*diol*.—The ester (253·5 g., 0·75 mol.) was reduced with lithium aluminium hydride and the resultant diol (168 g.) obtained by crystallisation from ethereal solution. The crude solid (50 g.) recovered from the mother-liquors was reprocessed with lithium aluminium hydride, to give a total quantity of 200 g. (94·5%) of *diol*, m. p. 108—109° (Found : C, 76·9; H, 11·9. $C_{18}H_{34}O_2$ requires C, 76·5; H, 12·1%). The *phenylurethane* derivative crystallised from methanol as fine needles, m. p. 171—172° (Found : C, 73·6; H, 8·4; N, 5·5. $C_{32}H_{44}O_4N_2$ requires C, 73·8; H, 8·5; N, 5·4%).

1 : 8-*Dibromo*-3 : 3-6 : 6-*di(pentamethylene)octane*.—The diol (188 g.) yielded crude dibromide which, being insoluble in light petroleum, was dissolved in hot benzene (2 l.). The solution was washed with hot water and sodium hydrogen carbonate solution and dried by distilling off the benzene. The residue crystallised from benzene–light petroleum, yieding 1 : 8-*dibromo*-3 : 3-6 : 6-*di(pentamethylene)octane* (216 g., 80%) as minute needles, m. p. 104·5—105·5° (Found : C, 53·0; H, 7·9; Br, 38·8. $C_{18}H_{32}Br_2$ requires C, 52·95; H, 7·9; Br, 39·15%).

3 : 3-6 : 6-*Di(pentamethylene)octane*.—The dibromide (184 g.) was reduced to the hydrocarbon by the prolonged action of zinc dust and refluxing acetic acid. The 3 : 3-6 : 6-*di*-(*pentamethylene*)*octane* (88 g., 78%), isolated as described previously, distilled as a colourless oil at 130°/0·8 mm. (Found : C, 86·1; H, 13·7. $C_{18}H_{34}$ requires C, 86·3; H, 13·7%).

Methyl Hydrogen 2 : 2-5 : 5-*Di*(*pentamethylene*)*hexane*-1 : 6-*dicarboxylate*.—This substance was prepared by partial hydrolysis of the dimethyl ester (400 g.) with acetic acid (145 g.) and hydrochloric acid (30 ml.). The mixture was refluxed in an oil-bath and the methyl acetate distilled off through a small column as it formed. When the theoretical quantity of methyl acetate had been removed, benzene (100 ml.) was added and the water removed as the benzene–water azeotrope. The residue was fractionated at reduced pressure, to give unchanged ester at 148°/0·6 mm., acid ester at 168°/0·6 mm., and a residue of diacid. This residue was combined with unchanged ester and heated to 180° till homogeneous; then it was cooled to 100° and hydrochloric acid and dibutyl ether were added in the proportions required for the acid ester synthesis (*Org. Synth.*, **19**, 45). After 5 hours' refluxing, the product was again isolated and fractionated, any diacid and diester being returned for further treatment. In this way the acid ester (280 g.) was obtained in 73% yield as a highly viscous oil

Dimethyl 2 : 2-5 : 5-8 : 8-11 : 11-*Tetra*(*pentamethylene*)*dodecane*-1 : 12-*dicarboxylate*.—The acid ester was electrolysed under the conditions already described and the product was fractionated in a spinning-band column. The final fraction (62 g.), b. p. 180—195°/0·05 mm., slowly deposited crystals of the required ester. On crystallisation from methanol, the *dimethyl* ester (35 g., 14·5%) formed large colourless needles, m. p. 94·5° (Found: C, 77·3; H, 11·1. $C_{36}H_{62}O_4$ requires C, 77·4; H, 11·2%). The corresponding *acid* crystallised from dioxan as a white powder, m. p. 202° (Found: C, 76·7; H, 11·0. $C_{34}H_{58}O_4$ requires C, 76·7; H, 11·0%).

3 : 3-6 : 6-9 : 9-12 : 12-*Tetra*(*pentamethylene*)*tetradecane*-1 : 14-*diol*.—The ester (30 g.) was reduced by lithium aluminium hydride (5 g.) in ether (600 ml.). The ester was not very soluble in ether and was therefore placed in the thimble of a Soxhlet extractor and dissolved by the refluxing solvent. The solution was finally concentrated. The *diol* (27 g.) separated as a powder, m. p. 117—118° (Found: C, 80·9; H, 12·2. $C_{34}H_{62}O_2$ requires C, 81·2; H, 12·4%).

1 : 14-*Dibromo*-3 : 3-6 : 6-9 : 9-12 : 12-*tetra*(*pentamethylene*)*tetradecane*.—The *dibromide* (30 g.) crystallised at low temperature from light petroleum as small needles, m. p. 99—100° (Found: C, 65·5; H, 9·5; Br, 25·3. $C_{34}H_{60}Br_2$ requires C, 65·0; H, 9·6; Br, 25·4%).

3 : 3-6 : 6-9 : 9-12 : 12-*Tetra*(*pentamethylene*)*tetradecane*.—The dibromide (24 g.) with zinc dust and glacial acetic acid gave 3 : 3-6 : 6-9 : 9-12 : 12-*tetra*(*pentamethylene*)*tetradecane* (10 g., 63%) which crystallised from methylene chloride at low temperature as fine needles, m. p. 70—71° (Found: C, 86·7; H, 13·2. $C_{34}H_{62}$ requires C, 86·7; H, 13·3%).

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251. *New Intermediates and Dyes. Part III.* Condensation of* 4-tert.-*Butylphthalic Anhydride with Acenaphthene.* 6-tert.-*Butylquinizarin and Derived Cellulose Acetate Dyes.*

By BRIAN W. LARNER and ARNOLD T. PETERS.

The carbonyl group *meta* to the *tert.*-butyl group in 4-*tert.*-butylphthalic anhydride reacts with acenaphthene in the Friedel–Crafts reaction, and the orientation of the derived carboxylic acid is established.

6-*tert.*-Butylquinizarin is synthesised from the anhydride by a variety of methods, and is converted into magenta and blue dyes for cellulose acetate rayon. *tert.*-Butyl-phenolphthalein, -fluorescein, and -eosin are prepared.

4-*tert.*-BUTYLPHTHALIC ANHYDRIDE (I) was converted into *tert.*-butyl-phenolphthalein and -fluorescein by fusion with phenol and resorcinol, respectively. Condensation probably occurred at both carbonyl groups of (I) to give mixtures.

Tetrabromination of *tert.*-butylfluorescein to the corresponding *tert.*-butyleosin afforded two main products, one of which retained alcohol tenaciously. The fluorescein and eosin derivatives give strong yellowish-green and greenish-yellow fluorescent solutions, respectively, in dilute aqueous alkali.

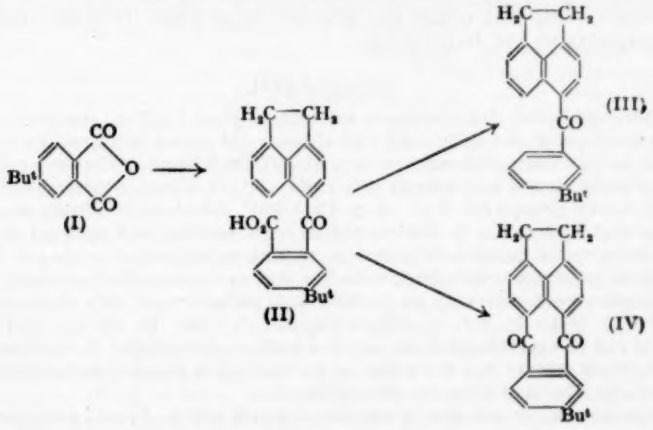
* Part II, *J.*, 1951, 680.

Friedel, Weizmann, and Wyler (*J.*, 1907, **91**, 1584) prepared fluorescein and eosin derivatives from 4-hydroxy- and 4-methoxy-phthalic anhydride, and the four compounds had indefinite melting points, suggestive of mixtures. Blicke and Smith (*J. Amer. Chem. Soc.*, 1929, **51**, 1865) prepared the phenolphthaleins from 4-halogenophthalic anhydrides, and estimated the proportions of isomerides by alkali fusion and separation of the resulting hydroxybenzoic acids; initial condensation had occurred mainly at the carbonyl group *meta* to the halogen atom.

Interaction of (I) and acenaphthene in the Friedel–Crafts reaction, in presence of aluminium chloride, with benzene as solvent, gave mainly 3-(5-*tert.*-butyl-2-carboxybenzoyl) acenaphthene (II), which was purified by passing dry hydrogen chloride through its solution in methyl alcohol for a short time, the crystalline product being "salted out"; further treatment with hydrogen chloride in alcohols gave excellent yields of the methyl and the ethyl ester, respectively. No isomerisation of (II) was noted in concentrated sulphuric acid (cf. Part II *). Decarboxylation of the carboxylic acid (II) by a trace of copper bronze in quinoline (Shepard, Winslow, and Johnson, *J. Amer. Chem. Soc.*, 1930, **52**, 2084) yielded the solid ketone, 3-*m*-*tert.*-butylbenzoylacenaphthene (III). The constitution of (III), and thus the orientation of (II), was shown by synthesis of (III) from acenaphthene and *m*-*tert.*-butylbenzoyl chloride in benzene, in presence of aluminium chloride; under the conditions recorded in Part II, it did not give an oxime. Synthesis of 3-acenaphthoic acid from 3-bromoacetylacenaphthene by the method of G.P. 479 916 (Friedländer, **16**, 516), using aqueous sodium hypochlorite, or of Fieser and Hershberg (*J. Amer. Chem. Soc.*, 1939, **61**, 1279), using potassium iodide and iodine in dioxan, failed, but that from acenaphthene and oxalyl chloride (Liebermann and Zsuffa, *Ber.*, 1911, **44**, 202) succeeded. Interaction of the acid chloride with the Grignard reagent from *m*-bromo-*tert.*-butylbenzene afforded an unidentified product. Acenaphthene and *p*-*tert.*-butylbenzoyl chloride in presence of aluminium chloride afforded 3-4′-*tert.*-butylbenzoylacenaphthene, an oil which gave a readily crystallised oxime.

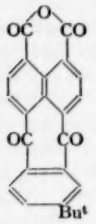
In the condensation of (I) with acenaphthene, the carbonyl group *meta* to the *tert.*-butyl is the main position of attack, and thus the nature of the hydrocarbon is also a determining factor in the reaction; *e.g.*, *tert.*-butylbenzene reacts with (I) mainly at the carbonyl group *para* to the *tert.*-butyl group (Part II).

Attempts to cyclise 3-(5-*tert.*-butyl-2-carboxybenzoyl)acenaphthene with sulphuric acid gave water-soluble sulphonic acids, but mixed aluminium and sodium chlorides (cf. Peters and Rowe, *J. Soc. Dyers and Col.*, 1943, **59**, 52) effected the required ring closure. Chromatographic purification of the resulting product gave a low yield of the yellow 3 : 4-(4-*tert.*-

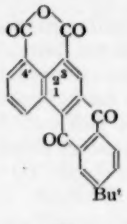


butylphthaloyl)acenaphthene (IV), which would have the same configuration whichever carbonyl group of (I) were the more reactive. The carboxylic acid (II) was oxidised by

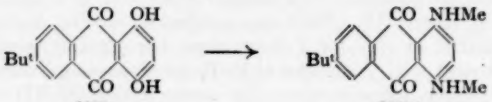
sodium dichromate in acetic acid to 4-(5′-*tert.*-butyl-2′-carboxybenzoyl)-1 : 8-naphthalic anhydride, which condensed with *o*-phenylenediamine to yield a benziminazole derivative. Compound (IV) was oxidised to 4 : 5-(4′-*tert.*-butylphthaloyl)-1 : 8-naphthalic anhydride (V); cyclisation of 4-(5′-*tert.*-butyl-2′-carboxybenzoyl)-1 : 8-naphthalic anhydride with 20% fuming sulphuric acid and boric acid was effected without sulphonation to give 7-*tert.*-butyl-1 : 2-benzanthraquinone-3 : 4′-dicarboxylic anhydride (VI), isomeric with (V).



(V)



(VI)



(VII) (VIII)

6-*tert.*-Butylquinizarin (VII) was synthesised in order to convert it into cellulose acetate rayon dyes, which were then compared with the commercial analogues from quinizarin. *tert.*-Butylphthalic anhydride (I) and *p*-chlorophenol in tetrachloroethane in presence of aluminium chloride yielded 6(or 7)-*tert.*-butyl-1-chloro-4-hydroxyanthraquinone, but no intermediate benzoylbenzoic acid was isolated. Ullmann and Schmidt (*Ber.*, 1919, **52**, 2098) converted 1-chloro-4-hydroxy-2-methylanthraquinone into 2-methylquinizarin by sulphuric acid and boric acid at 160°, and a similar hydrolysis of 1-chloro-4-hydroxyanthraquinone to quinizarin is recorded in G.P. 203 083. We found that, in a similar manner, 6(or 7)-*tert.*-butyl-1-chloro-4-hydroxyanthraquinone afforded 6-*tert.*-butylquinizarin which was purified by chromatographic absorption on alumina, or by sublimation in high vacuum, to give bright red needles. The latter was also prepared directly by condensing the anhydride (I) with *p*-chlorophenol or quinol in presence of sulphuric and boric acids at 210° or, better, by the use of a melt of aluminium and sodium chlorides, as recorded by Mayer and Gunther (*Ber.*, 1930, **63**, 1455) and by Mayer and Stark (*Ber.*, 1931, **64**, 2003) for the preparation of 6- and 5-methylquinizarin from the respective methylphthalic anhydride and quinol.

Compound (VII) was converted into the diamino- and the bis-methylamino-anthraquinone (VIII) when heated with sodium dithionite (hydrosulphite) and aqueous ammonia or methylamine, respectively. The bases dye cellulose acetate rayon deep magenta and blue, respectively, somewhat redder and greener, respectively, than the shades given by analogues containing no *tert.*-butyl group.

Experimental

tert.-*Butylphenolphthalein.*—An intimate mixture of phenol (37 g., 0·4 mol.), 4-*tert.*-butylphthalic anhydride (20 g., 0·1 mol.), and zinc chloride (54 g., 0·4 mol.) was heated at 120° for 2 hours, raised to 160° during 1 hour, and kept at 160° for 3 hours. The deep red mixture was poured into absolute alcohol and filtered (charcoal), and the filtrate concentrated; after separation of a pale brown precipitate (8 g.), m. p. 295—305°, the alcoholic filtrate was diluted with water and distilled with steam to remove phenol; the residual buff-coloured precipitate was collected and extracted with warm 10% aqueous sodium carbonate to remove *tert.*-butylphthalic acid, the insoluble residue was dissolved in alcohol, and water was added carefully to precipitate an almost colourless product (18 g.), m. p. 300—313° (mixed m. p. with above product, 300—307°) (Found: C, 76·4; H, 6·1. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9%). tert.-*Butylphenolphthalein* could not be crystallised from any of a variety of solvents; it dissolves in sulphuric acid with a deep red colour; the red colour of its solution in aqueous sodium hydroxide has a slightly bluer tinge than that given by phenolphthalein.

tert.-*Butylfluorescein.*—4-*tert.*-Butylphthalic anhydride (5·1 g., 1 mol.) and resorcinol (5·5 g., 2 mols.) were ground and fused; freshly powdered anhydrous zinc chloride (2 g.) was added with stirring, and the temperature was raised to 200° during 1 hour; much frothing accompanied elimination of water. After 1 hour at 200°, the mass became almost solid; it was cooled

and digested with hydrochloric acid (2·5 c.c.) and water (50 c.c.), and the yellow solid (8·1 g., 82%) was collected and crystallised several times from alcohol, to give yellow prisms, m. p. 332—340° (Found: C, 73·7; H, 5·2. $C_{24}H_{20}O_5$ requires C, 74·2; H, 5·15%). The colour and fluorescence of tert.-*butylfluorescein* in dilute caustic alkalis are similar to those shown by fluorescein.

tert.-*Butyleosin*.—Bromine (8 g.) was added slowly to a suspension of *tert.*-butylfluorescein (4 g.) in absolute alcohol (20 c.c.) at room temperature. Heat was developed; after all the bromine had been added (20 minutes) and the whole kept for a further hour, orange prisms of the *eosin*, m. p. 314° (decomp.) (1·2 g.), were collected (Found: C, 40·2; H, 2·6; Br, 44·0. $C_{24}H_{16}O_5Br_4$ requires C, 40·9; H, 2·3; Br, 45·4%). The filtrate yielded orange-red prisms (2·7 g.) of a *solvate*, m. p. 248·5—249° (sharply), which retained alcohol tenaciously (Found: C, 42·4; H, 3·6; Br, 41·4. $C_{24}H_{16}O_5Br_4,2C_2H_5{\cdot}OH$ requires C, 42·2; H, 3·5; Br, 40·2%).

3-(5′-tert.-*Butyl-2′-carboxybenzoyl)acenaphthene*.—Anhydrous aluminium chloride (13·3 g., 2 mols.) was added to a stirred solution of 4-*tert.*-butylphthalic anhydride (10·2 g., 1 mol.) and acenaphthene (7·7 g., 1 mol.) in dry benzene (250 c.c.) at <30°. After reaction had moderated, the mixture was left overnight at room temperature and the resulting complex decomposed with dilute hydrochloric acid; benzene and a little acenaphthene were distilled with steam, and the insoluble residue was collected and extracted with boiling 10% aqueous sodium carbonate (500 c.c.); acidification of the alkaline extract (after treatment with charcoal) gave an almost colourless solid (14·2 g., 80%), which crystallised from aqueous acetic acid in colourless needles, m. p. 260° (decomp.); on dissolution of the latter in methyl alcohol and passage of hydrogen chloride through the cold solution, the alkali-soluble 3-(5′-tert.-*butyl-2′-carboxybenzoyl)acenaphthene* separated in colourless, prismatic needles, m. p. 271—273° (Found: C, 80·0; H, 6·0. $C_{24}H_{22}O_3$ requires C, 80·4; H, 6·1%). If further hydrogen chloride was introduced, the carboxylic acid dissolved and the resulting pale orange solution on concentration yielded the *methyl* ester, which crystallised from methyl alcohol in pale yellow prisms, m. p. 139—140° (Found: C, 80·3; H, 6·3. $C_{25}H_{24}O_3$ requires C, 80·6; H, 6·5%), insoluble in aqueous ammonia. The *ethyl* ester, prepared similarly, crystallised from alcohol in yellow cubes, m. p. 123—124° (Found: C, 80·8; H, 6·6. $C_{26}H_{26}O_3$ requires C, 80·8; H, 6·7%).

1- *and* 3-*Acetylacenaphthene* (method: Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1939, **61**, 1272).—Aluminium chloride (84 g.), acenaphthene (90 g.), and acetyl chloride (45 c.c.) in dry nitrobenzene gave acenaphthene (3·1 g.), b. p. 130—146°/0·7 mm., and a mixture of 1- and 3-acetylacenaphthene (87·7 g., 78%), b. p. 146—147°/0·7 mm., m. p. 62°.

1- *and* 3-*Bromoacetylacenaphthene* (method: Nightingale *et al.*, *J. Amer. Chem. Soc.*, 1945, **67**, 1262).—The mixed acetylacenaphthenes (19·4 g., 1 mol.) and bromine (16 g., 2 mols.) in dry ether gave a yellow precipitate (5·1 g.), which crystallised from chloroform in colourless prisms of 1-bromoacetylacenaphthene, m. p. 163—164°, darkening in air. The ethereal filtrate was washed with aqueous sodium hydrogen sulphite and then sodium hydrogen carbonate, and water, to yield, on removal of ether, a sticky solid, which crystallised from methyl alcohol in yellow needles, m. p. 84—86°, of 3-bromoacetylacenaphthene (7 g.).

3-*Acenaphthoic Acid* (method: Liebermann and Zsuffa, *loc. cit.*).—Acenaphthene (2 g.) and oxalyl chloride (6 g.) at 140° in a sealed tube gave the acid, which was purified through aqueous sodium carbonate and crystallised from aqueous acetic acid in bright yellow prisms (1·4 g.), m. p. 217—218°. The acid (2 g.) was converted by thionyl chloride into the acid chloride, m. p. 118—120°, and treatment with the Grignard reagent from *m*-bromo-*tert.*-butylbenzene (2·2 g.) and magnesium (0·25 g.) in ether afforded a product, b. p. 185°/0·7 mm., which crystallised from alcohol in colourless prisms, m. p. 170—172°, not identical with 3-*m-tert.*-butylbenzoylacenaphthene (see below).

3-m-tert.-*Butylbenzoylacenaphthene*.—Acenaphthene (3·8 g., 1 mol.), *m-tert.*-butylbenzoyl chloride (5 g., 1 mol.), and aluminium chloride (5 g., 1·5 mols.) in dry benzene (30 c.c.) at room temperature for 5 hours, and then at the b. p. for 30 minutes, gave 3-m-tert.-*butylbenzoylacenaphthene*, which crystallised from benzene–ligroin (b. p. 60—80°) in colourless prisms, m. p. 110° (3·2 g., 41%) (Found: C, 88·3; H, 7·0. $C_{23}H_{22}O$ requires C, 87·9; H, 7·0%).

Decarboxylation of 3-(5-tert.-*Butyl-2-carboxybenzoyl)acenaphthene*.—The carboxylic acid (4 g.) was heated with quinoline (10 c.c.) and copper bronze (0·4 g.) at 215—220° for 30 minutes; after filtration and addition to excess of aqueous hydrochloric acid (1 : 1), the residue (2·8 g., 85%) was extracted with warm dilute sodium carbonate solution, dried, and crystallised from ligroin (b. p. 60—80°) or benzene–ligroin in colourless prisms, m. p. 110—111°, which did not depress the m. p. of 3-*m-tert.*-butylbenzoylacenaphthene as prepared above.

3-p-tert.-*Butylbenzoylacenaphthene*.—Acenaphthene (7·7 g., 1 mol.) and *p-tert.*-butylbenzoyl

chloride (10 g., 1 mol.) were dissolved in dry benzene (50 c.c.), and aluminium chloride (10 g., 1·5 mols.) was added gradually, with stirring, at room temperature. After 3 hours, the crimson mixture was refluxed for 15 minutes, cooled, and decomposed, the benzene layer was separated, and the *p-tert.*-butyl derivative distilled as a pale yellow oil (10·1 g., 65%), b. p. 280°/6 mm.; the ketone was converted into the *oxime*, which crystallised from benzene–ligroin (b. p. 60—80°) in colourless prisms, m. p. 175—177° (Found: C, 83·5; H, 7·1; N, 4·4. $C_{23}H_{23}ON$ requires C, 83·9; H, 7·0; N, 4·3%).

3 : 4-(4-tert.-*Butylphthaloyl*)*acenaphthene* (IV).—The use of fuming sulphuric acid gave soluble sulphonated products only. The carboxylic acid (II) (7·2 g.) was ground with anhydrous aluminium chloride (24 g.) and sodium chloride (6 g.), and the mixture heated at 130° for 30 minutes, and then at 140° for 30 minutes; decomposition with dilute hydrochloric acid, followed by extraction of the resulting precipitate with 10% aqueous sodium carbonate at 50° for 2 hours, gave a dark brown insoluble residue; this was chromatographed (benzene–alumina) to give, by elution of the yellow band with benzene, removal of solvent, and crystallisation of the residue twice from alcohol, yellow prisms (1·2 g., 18%), m. p. 188—189°, of **3 : 4-(4′-tert.-*butylphthaloyl*)*acenaphthene*** (Found: C, 85·0; H, 6·1. $C_{24}H_{20}O_2$ requires C, 84·7; H, 5·9%).

4 : 5-(4-tert.-*Butylphthaloyl*)-1 : 8-*naphthalic Anhydride* (V).—Powdered sodium dichromate (8 g.) was added carefully to a solution of **3 : 4-(4′-*tert.*-**butylphthaloyl)acenaphthene (2 g.) in boiling acetic acid (60 c.c.); after 4 hours' refluxing and addition to ice-water, the resulting precipitate was collected and extracted with boiling 10% aqueous sodium carbonate and filtered (charcoal). Acidification of the alkaline extract gave a precipitate, which was crystallised several times from aqueous acetic acid, to give stout, pale yellow prisms (0·6 g., 27%), m. p. 310°, of the ***anhydride*** (Found: C, 74·6; H, 4·2. $C_{24}H_{16}O_5$ requires C, 75·0; H, 4·2%).

4-(5-tert.-*Butyl*-2-*carboxybenzoyl*)-1 : 8-*naphthalic Anhydride*.—**3-(5-*tert.*-**Butyl-2-carboxybenzoyl)acenaphthene (3·6 g.) was heated with sodium dichromate (10 g.) in acetic acid (75 c.c.) for 6 hours. The resulting product, isolated as usual, crystallised from aqueous acetic acid in yellow prisms, m. p. 238—240°, of the ***naphthalic anhydride*** (2·9 g., 72%) (Found: C, 71·3; H, 4·7. $C_{24}H_{18}O_6$ requires C, 71·6; H, 4·5%). Heating the anhydride with *o*-phenylenediamine in boiling acetic acid for 15 minutes gave orange needles, m. p. 300—302°, of the ***benziminazole*** derivative (Found: N, 5·9. $C_{30}H_{22}O_4N_2$ requires N, 6·0%).

7-tert.-*Butyl*-1 : 2-*benzanthraquinone*-3 : 4′-*dicarboxylic Anhydride* (VI).—**4-(5-*tert.*-**Butyl-2-carboxybenzoyl)-1 : 8-naphthalic anhydride (2 g.), boric anhydride (2 g.), and 20% fuming sulphuric acid (6 c.c.) were heated at 140—160° during 4 hours. The resulting thick mass was cooled and diluted with water, and the dark green precipitate was extracted three times with warm 10% aqueous sodium carbonate (200 c.c.); the insoluble residue crystallised from acetic acid and then from nitrobenzene in yellowish-green prisms, m. p. 286°, of the ***benzanthraquinone*** (0·3 g., 16%) (Found: C, 74·5; H, 3·9. $C_{24}H_{16}O_5$ requires C, 75·0; H, 4·2%), isomeric with the above **4 : 5-(4-*tert.*-**butylphthaloyl)-1 : 8-naphthalic anhydride.

Condensation of the Anhydride* (I) *with* p-*Chlorophenol*.**—(i) **6(or 7)-tert.-*Butyl*-1-*chloro*-4-*hydroxyanthraquinone*.** Anhydrous aluminium chloride (13·3 g.) was added in portions to a solution of **4-*tert.*-**butylphthalic anhydride (12·8 g.) and *p*-chlorophenol (6·4 g.) in tetrachloroethane (30 c.c.). The stirred mixture was heated on the steam-bath for 3 hours, and the resulting deep crimson solution was added to water, and the tetrachloroethane distilled with steam. The residual dark oily mass was extracted with dilute aqueous ammonia, and the insoluble residue (2 g.) crystallised from acetic acid and then alcohol in greenish-yellow needles, m. p. 150—152°, of **6(or 7)-tert.-*butyl*-1-*chloro*-4-*hydroxyanthraquinone (Found: C, 68·9; H, 4·4; Cl, 11·55. $C_{18}H_{13}O_3Cl$ requires C, 68·6; H, 4·8; Cl, 11·3%). Although considerable amounts of starting materials were recovered from the above reaction, no intermediate chloro-carboxylic acid was isolated. Using a similar method with tetrachlorophthalic anhydride, Ullmann and Schmidt (*Ber.*, 1919, **52**, 2098) isolated an intermediate benzoylbenzoic acid derivative, with a trace of the cyclised anthraquinone.

(ii) **6-tert.-*Butylquinizarin*.** Boric acid (6 g., 1 mol.) was dissolved in 98% sulphuric acid (68 c.c.) by stirring at 50°; to the solution were added **4-*tert.*-**butylphthalic anhydride (15·3 g., 0·75 mol.) and *p*-chlorophenol (6·4 g., 0·5 mol.), alternately, in portions during 1 hour at 50°, to yield a pale brown solution. The temperature was then raised to 160° during 2 hours, and kept at 160° for a further 3 hours; then it was raised to 210° during 1 hour and kept at this temperature for a further 2 hours (this procedure is essential for good yields). After cooling to 100°, 98% sulphuric acid (20 c.c.) and water (33 c.c.) were added and the mixture poured on ice; the precipitated boric ester was decomposed by boiling it with water (300 c.c.) for 10 minutes. The resulting brown product was collected and extracted with boiling 2% aqueous sodium

hydroxide, and acidification of the extract gave a dark brown mass (7 g.), which was crystallised from dry chlorobenzene in chlorine-free reddish-orange prisms (2·2 g.), m. p. 169—171°. Pure 6-tert.-*butylquinizarin* was obtained by sublimation at 2 mm., to give bright red prismatic needles, m. p. 173° (Found: C, 72·7; H, 5·1. $C_{18}H_{16}O_4$ requires C, 72·9; H, 5·4%). The above 6(or 7)-*tert.*-butyl-1-chloro-4-hydroxyanthraquinone (0·8 g.) was added to a solution of boric acid (6 g.) in 98% sulphuric acid (8 c.c.), and the deep red solution heated in an oil-bath at 190° for 6 hours. The colour became bluer, and, on addition to ice-water, 6-*tert.*-butylquinizarin (0·6 g., 80%), m. p. and mixed m. p. 169—171°, was obtained.

Condensation of the Anhydride (I) *with Quinol.*—(*a*) The above experiment (i), in which tetrachloroethane was used as solvent, was repeated, with quinol (5·5 g.) in place of *p*-chlorophenol. After extraction of the resulting product with dilute aqueous ammonia, the dry purple substance was extracted with benzene and the solution poured through a column of alumina; development with benzene gave a soluble yellow fraction, and the deep maroon band, due to 6-*tert.*-butylquinizarin was eluted very slowly even with benzene–alcohol. Complex formation had occurred, and the band was removed and extracted with boiling acetic acid to yield 6-*tert.*-butylquinizarin (2·1 g.), m. p. and mixed m. p. 169—171°. Again, no trace of intermediate benzoylbenzoic acid was detected.

(*b*) The above experiment (ii) was repeated with *p*-chlorophenol replaced by quinol (5·5 g.). The reaction gave quinol and 6-*tert.*-butylquinizarin (1·5 g.).

(*c*) Simultaneous condensation and cyclisation were effected by the use of a sodium chloride–aluminium chloride melt, which proved to be the most convenient method. 4-*tert.*-Butylphthalic anhydride (26 g.) and quinol (11 g.) were added gradually to a stirred melt of sodium chloride (10 g.) and aluminium chloride (50 g.) at 130°; the mixture was carefully heated to 140° and, after 5 hours at this temperature, the red semi-solid mass was added to ice and dilute hydrochloric acid, and the mixture was boiled. On cooling, the solid was collected and crystallised from acetic acid in orange-red prisms, m. p. 170—171°, of 6-*tert.*-butylquinizarin (6·5 g.).

1 : 4-*Diamino*-6-tert.-*butylanthraquinone.*—The method of preparation was similar to that used by Mayer and Stark (*Ber.*, 1931, **64**, 2003) for the unsubstituted analogue. 6-*tert.*-Butylquinizarin (2 g.), sodium hydrosulphite (dithionite) (2 g.), and aqueous ammonia (*d* 0·88; 12 c.c.) were heated in a sealed tube at 145—150° for 7 hours. The resulting mixture was diluted with water and the collected solid, which may have contained some leuco-compound of the dye, was washed with hot 5% aqueous sodium hydroxide and water, and dried, to give a deep violet powder (1·8 g., 90%), m. p. 200—220°. Sublimation at 3 mm. gave violet needles, m. p. 223—224°, with a coppery lustre (Found: C, 73·4; H, 6·2; N, 9·2. $C_{18}H_{18}O_2N_2$ requires C, 73·4; H, 6·1; N, 9·5%). 1 : 4-*Diamino*-6-tert.-*butylanthraquinone* dyes cellulose acetate rayon a deep magenta shade. The sample was milled with "Tannadol" and water and dyed at 65—85°; 0·5 and 2% shades were redder and duller than those given by 1 : 4-diaminoanthraquinone, but were slightly more resistant to gas-fume fading.

6-tert.-*Butyl*-1 : 4-*bismethylaminoanthraquinone* (VIII).—6-*tert.*-Butylquinizarin (1 g.), sodium dithionite (1 g.), and 33% aqueous methylamine (6 c.c.) at 145—150° for 7 hours, followed by vacuum sublimation (3 mm.) of the resulting product, gave the *dye* (1·8 g., 88%) as dark blue crystals, m. p. 142°, with a bronze lustre (Found: C, 75·0; H, 6·9; N, 8·5. $C_{20}H_{22}O_2N_2$ requires C, 74·5; H, 6·8; N, 8·5%). The cellulose acetate rayon dyeings were a greener and duller blue than those shown by the analogous 1 : 4-bismethylamino-derivative, and possessed similar gas-fume fading fastness.

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252. *The Spectrophotometric Determination of the Ionisation Constants of Aromatic Nitro-compounds.*

By J. C. D. Brand, W. C. Horning, and M. B. Thornley.

The ultra-violet absorption spectrum of aromatic nitro-compounds is modified characteristically in powerfully acid (H_2SO_4 and H_2SO_4–SO_3) solvents by the transfer of a proton to the nitro-group, yielding ions of the formula $Ar{\cdot}NO{\cdot}OH^+$, with alteration of the binding energies (but not the number) of the π-electrons. The ionisation constants have been evaluated from the spectra in sulphuric acid media. Simple mononitro-compounds are weak bases in anhydrous sulphuric acid, but are quantitatively ionised in concentrated oleums. Di- and tri-nitro-compounds are much less basic and are incompletely ionised in the most powerfully acid oleum media. In terms of H_0, the acidity of the oleums falls 3 units below that of anhydrous sulphuric acid.

The influence of substituents on the ionisation constant is generally in semi-quantitative agreement with the electrostatic theory, but the entropy of ionisation shows that environmental factors are not inappreciable. Attention is drawn to the discrepancy between the ionisation constants reported here and those obtained by cryoscopic methods (Gillespie, *J.*, 1950, 2542), and the reasons for this are discussed.

All mononitro-derivatives of benzene behave as weak bases in sulphuric acid solution. The ions formed, $Ar{\cdot}NO{\cdot}OH^+$, are isoelectronic with derivatives of benzoic acid, but are more powerfully acidic owing to the formal charge on the central nitrogen atom and the large resonance energy associated with the nitro-group. As a class they are the strongest cation acids about which there is reasonably quantitative information. The basicity of the nitro-group was discovered cryoscopically by Hantzsch in 1908 (*Z. physikal. Chem.*, **65**, 41) and approximate ionisation constants were later evaluated by this method (Hammett, *J. Chem. Physics*, 1940, **8**, 644; Gillespie, *J.*, 1950, 2542). Ionisation constants may also be determined from the ultra-violet spectrum, which is modified in a regular, characteristic fashion by the transfer of the proton (Brand, *J.*, 1950, 997). No other general methods seem to be available at present.

The cryoscopic and optical methods both have important limitations. Cryoscopy can be used in sulphuric acid containing a trace of water, but is not adaptable outside the limits of a narrow range of solvent composition. For the present purpose this operates rather unfavourably because the degree of ionisation of bases weaker than nitrobenzene itself is inconveniently low in such media. The optical method has a free choice of medium, but suffers from the disadvantage that it is necessary to know the spectrum of the conjugate ion of the nitro-compound. The very feebly basic trinitro-compounds, for example, are too incompletely ionised, even in the most strongly acid medium, to be treated quantitatively. In addition, quite serious difficulties arise from the physical influence of a change of medium on the spectra. These disadvantages are at least partly offset by the access to a useful range of media in which H_0 falls 3 units below that of anhydrous sulphuric acid. The ionisation constants of several nitro-compounds have now been evaluated in these mixtures.

The characteristic spectral effect of the proton is to move the principal absorption band some 6000—9000 cm.$^{-1}$ towards lower frequencies and simultaneously to increase $\varepsilon_{max.}$ nearly two-fold. Weaker bands on the long wave-length shoulder are also displaced, and may remain prominent or disappear, depending on other substituents present in the molecule (Figs. 1—6). The main band must represent the same transition in the ion and the uncharged molecule, which have the same π-electron configuration, and it has been suggested that it corresponds to the transition of benzene at 50 000 cm.$^{-1}$ (Doub and Vandenbelt, *J. Amer. Chem. Soc.*, 1947, **69**, 2714; 1949, **71**, 2414; Platt, *J. Chem. Physics*, 1951, **18**, 101). This assignment meets with the following difficulty. In the spectrum of

the univalent ion of 2 : 4-dinitrotoluene (Fig. 1, broken curve) *two* intense bands are present, the first with the frequency and intensity characteristic of the ion of a mononitro-compound (3500 Å), and the second characteristic of an un-ionised mononitro-compound (2650 Å). The evidence from the spectrum of 2 : 4-dinitrochlorobenzene is similar, but less complete, and in either case the absorption is quite different from that of an ionised mononitro-compound (*e.g.*, *m*-nitroaniline cation, Fig. 2, curve *e*). The simplest interpretation is that the 40 000 cm.$^{-1}$ transition of nitrobenzene does not involve the benzene orbitals but

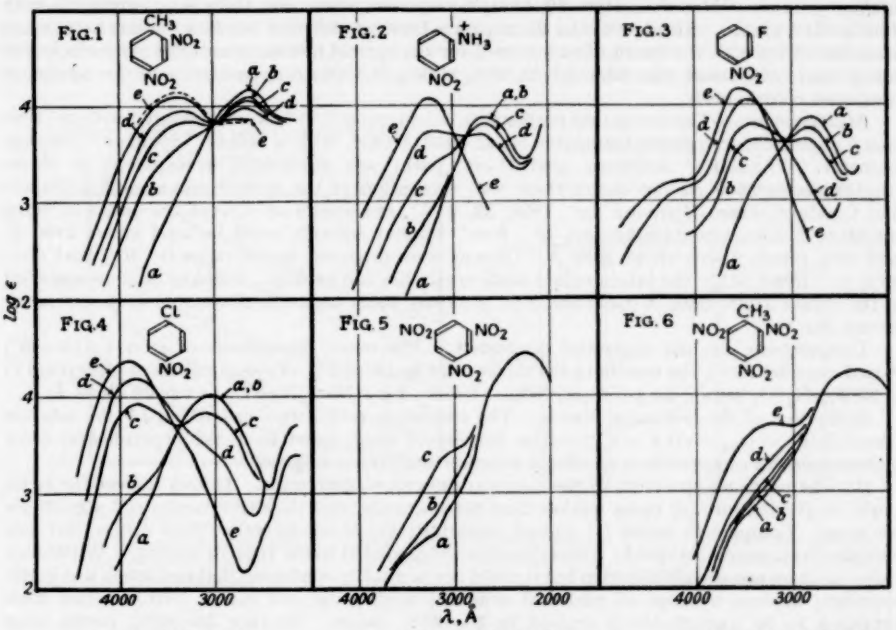


FIG. 1.
- *a*, 99·0% H_2SO_4.
- *b*, 102·74 ,,
- *c*, 105·46 ,,
- *d*, 107·30 ,,
- *e*, 114·5 ,,
- – – – calc. for ion.

FIG. 2.
- *a*, 99·1% H_2SO_4.
- *b*, 101·2 ,,
- *c*, 104·16 ,,
- *d*, 107·3 ,,
- *e*, 114·5 ,,

FIG. 3.
- *a*, 98·1% H_2SO_4.
- *b*, 100·81 ,,
- *c*, 101·88 ,,
- *d*, 105·78 ,,
- *e*, 114·5 ,,

FIG. 4.
- *a*, 97·8% H_2SO_4.
- *b*, 99·81 ,,
- *c*, 100·19 ,,
- *d*, 101·47 ,,
- *e*, 107·35 ,,

FIG. 5.
- *a*, 101·0% H_2SO_4.
- *b*, 108·3 ,,
- *c*, 114·5 ,,

FIG. 6.
- *a*, 99·0% H_2SO_4.
- *b*, 102·1 ,,
- *c*, 105·5 ,,
- *d*, 108·3 ,,
- *e*, 114·5 ,,

is localised mainly in the nitro-group, a suggestion which has been advanced previously to account for the photochemical formation of nitrosobenzene (Matsen and Hastings, *J. Amer. Chem. Soc.*, 1948, **70**, 3514). On this view the transition becomes $\mathbf{2a_2} \times \mathbf{2b_2}$ ($^1A_1 - {}^1B_1$), allowed by the electronic selection rules with polarisation perpendicular to the symmetry axis of the molecule. " Mixed " transitions of π-electrons from the upper, filled level ($\mathbf{2a_2}$) of the nitro-group to unfilled benzenoid levels may account for two of the weak, partially submerged transitions at longer wave-lengths where certainly two, possibly four, weak bands can be observed. The " mixed " transitions are allowed by the symmetry selection rules but are weakened by small overlap.

Experimental

Materials.—The preparation, storage, and analysis of the media were as described by Brand (*loc. cit.*). Measurement of the electrical conductivity was adopted for the more accurate

analysis of dilute oleum and concentrated sulphuric acid. The conductivity was determined at 25° ±0·005° in a U-shaped cell, bright platinum electrodes and a screened A.C. bridge (James and Knox, *Trans. Faraday Soc.*, 1950, **46**, 254) being used, and was stable and reproducible for several days. The measuring frequency was 1000—3000 cycles per second, and the cell was standardised by using Jones and Bradshaw's 0·1M-potassium chloride solution. Existing measurements of conductivity (Reinhardt, *J. Amer. Chem. Soc.*, 1950, **72**, 3359, where earlier references are given) are in very poor agreement with one another. Our results agree, within a few units %, with those of Bergius (*Z. physikal. Chem.*, 1910, **72**, 338) for fuming acids and of Lichty (*J. Amer. Chem. Soc.*, 1908, **30**, 1834) for aqueous acids; but there is no agreement with Reinhardt's figures. In view of the discrepancy between different workers, calibration curves were drawn up with the batch of oleum used for the optical measurement, the same electrodes being used; the oleum was diluted with 90% H_2SO_4 in a closed apparatus, and the resistance measured continuously.

Measurements.—The extinction coefficients, ε (cm. mole $l.^{-1})^{-1}$, were measured with a 'Unicam' photoelectric spectrophotometer or, at 3650 Å only, with a Hilger "Spekker" Absorptiometer. "AnalaR" Sulphuric acid (1-cm. path) was adequately transparent at wave-lengths above 2000 Å. In oleum there was absorption of the shorter wave-lengths (Fajans and Goodeve, *Trans. Faraday Soc.*, 1936, **32**, 511); the minimum solvent transmission being set at 50%, oleum containing 26% of "free" sulphur trioxide could be used above 2400 Å, and 65% oleum above about 2850 Å. Oleums were prepared in the range 0—36% and 60—65% of "free" SO_3; the intermediate acids crystallise too readily. Sulphur dioxide absorbed in the region 3100—2500 Å (Gold and Tye, *J.*, 1950, 2932), and was eliminated as described by Brand (*loc. cit.*).

Temperature was not controlled accurately. The mean dependence of ε on T (15—45°) varied considerably; the results in the tables refer to 18° ±2°. Typical values of $(1/\varepsilon)(d\varepsilon/dT)$ in 99·9% H_2SO_4 were: for *p*-$F{\cdot}C_6H_4{\cdot}NO_2$, +0·008; for *p*-$Me{\cdot}C_6H_4{\cdot}NO_2$, +0·0005 (3650 Å).

Evaluation of the Ionisation Ratios.—The ionisation ratios were calculated by the relation $[\text{Base}]/[\text{Ion}] = (\varepsilon_{\text{ion}} - \varepsilon)/(\varepsilon - \varepsilon_{\text{base}})$. The sources of error, apart from the experimental error of measurement of ε, which is relatively unimportant, are as follows.

(1) The reference spectrum of the ions was difficult to determine. In this respect the bases could be divided into (*a*) bases weaker than nitrobenzene, and (*b*) nitrobenzene and alkylnitrobenzenes. Compounds under (*b*) ionised quantitatively in moderately dilute oleum, but sulphonated at appreciable speed: ε was therefore extrapolated to the time of mixing. With bases under (*a*) there was no sulphonation but it could not be readily confirmed that ionisation was really complete, because a range of media of sufficient acidity did not exist. Nitrobenzene itself appeared to be quantitatively ionised in 30—36% oleum. Because 36—60% media were excluded, the closest approach to the ions of the weaker bases was in 60—65% oleum, in which H_0 was about 0·8 unit lower than in 36% oleum. Calculations with *m*- and *p*-chloro- and -fluoronitrobenzene were based on a reference spectrum in this medium, but the ionisation of 2 : 4-dinitrotoluene (and weaker bases) was still incomplete.

(2) A rising concentration of sulphur trioxide displaces the reference spectra of base and ion along the wave-length axis towards longer wave-lengths, with little alteration of the shape of the curves or the value of $\varepsilon_{max.}$ (Flexser, Hammett, and Dingwall, *J. Amer. Chem. Soc.*, 1935, **57**, 2103). The effect can be minimised therefore by working at a wave-length of maximum absorption. However, it is doubtful if this simple medium effect holds in the strong (65%) oleum, where formation of $Ar{\cdot}NO_2{,}SO_3$ in place of, or in equilibrium with, $Ar{\cdot}NO{\cdot}OH^+$ is probable.

Measurements were usually made at the absorption maximum of the ion. This has two advantages: the change of ε is greater and the medium is transparent, even with the strongest oleums. In some cases readings were taken at both maxima.

Calculation of Ionisation Constants.—Ionisation ratio, acidity function, and ionisation constant are related by the equation $H_0 = pK_a + \log_{10}[\text{Base}]/[\text{Ion}]$, where $K_a = a_{H^+}a_{\text{base}}/a_{\text{ion}}$, the activities referring to the standard state of an infinitely dilute aqueous solution (Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721). The ionisation ratio of the bases was plotted as a function of the medium composition (Fig. 7), and the acidity function of the fuming sulphuric acid (Fig. 8) determined from this group of approximately parallel curves. The numerical values are based on the figure $pK_a = -10{\cdot}34$ for the *p*-toluylnitracidium ion,* obtained in slightly aqueous media. In view of the long, stepwise derivation of H_0 and pK_a the accuracy, in the *absolute* sense, is probably low.

* Conjugate ions of the nitro-compounds are conveniently termed "nitracidium ions."

Some results are collected in Tables 1—3. Individual cases are referred to below.

Nitrobenzene and p-*Nitrotoluene* (Table 1).—The extinction coefficients at 3650 Å were reported by Brand (*loc. cit.*). In both cases the wave-length falls on a sloping part of the spectrum and the measurements have been repeated at the maximum of the nitracidium ions. In 99—100% H_2SO_4 the results are consistent with the H_0 data obtained by Hammett and Deyrup (*loc. cit.*) with the indicator 2 : 4 : 6-trinitroaniline.

m- *and* p-*Chloro- and -Fluoro-nitrobenzene* (Figs. 3 and 4).—The conclusion was formed from the values of ϵ at 3650 Å (Brand, *loc. cit.*) that ionisation of *p*-chloronitrobenzene was complete in 25% oleum. The new ionisation ratios are significantly different from the old, and this conclusion is now corrected. To obtain further information on the medium effect, the ionisation ratios of each of the bases were determined at the maxima of both the ion and the uncharged molecule. The ratios evaluated from the absorption of the base were then found to be about

FIG. 7. *Ionisation ratios in oleum media.*

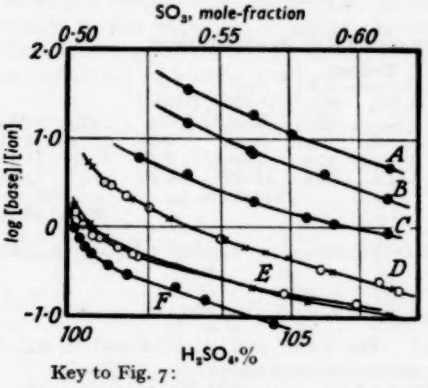
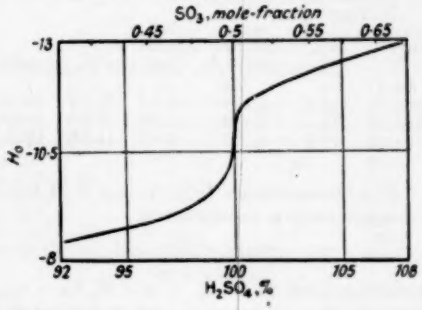


FIG. 8. *Acidity function of oleum.*



Key to Fig. 7:

A. 2 : 4-*Dinitrochlorobenzene*.
B. m-*Nitroaniline cation*.
C. 2 : 4-*Dinitrotoluene*.
D. × m-*Chloronitrobenzene*. ⊙ m-*Fluoronitrobenzene*.
E. × p-*Chloronitrobenzene*. ⊙ p-*Fluoronitrobenzene*.
F. *Nitrobenzene*.

0·1 unit lower than those obtained from the maximum of the ion. The difference, which is not explained if ionisation is incomplete in the 65% oleum, can be understood if the medium effect of the 65% acid is less simple than in dilute oleums and produces (besides the wave-length shift) an increase in ϵ, and hence leads to values of ϵ_{ion} which are a few units % too high. The exaltation of intensity has a larger effect on the ionisation ratio calculated from the absorption of the nitracidium ion. It would not be difficult to make the results self-consistent by adopting

TABLE 1. *Ionisation ratios and acidity constant of* p-*nitrotoluene.*

Medium						Medium					
H_2SO_4, %	SO_3, %	ϵ_{mean} (λ 3750 —3800 Å)	log [Base]/[Ion]	$-H_0$ *	$-pK_a$	H_2SO_4, %	SO_3, %	ϵ_{mean} (λ 3730 —3800 Å)	log [Base]/[Ion]	$-H_0$	$-pK_a$
93·5	—	1 460	—	—	—	100·04	0·18	16 370	−0·74	11·09	10·35
96·65	—	2 245	1·33	8·97	10·30	100·09	0·40	16 670	−0·80	11·16	10·36
98·98	—	4 370	0·70	9·60	10·30	100·11	0·49	16 810	−0·83	11·19	10·36
99·27	—	5 380	0·54	9·75	10·29	100·21	0·93	17 280	−0·94	11·32	10·38
99·42	—	5 750	0·49	9·83	10·34	100·31	1·38	17 650	−1·05	11·41	10·36
99·53	—	6 400	0·41	9·93	10·34	102·16	9·6	19 050	—	—	—
99·65	—	7 360	0·30	10·04	10·34	102·43	10·8	19 090	—	—	—
99·73	—	8 200	0·21	10·14	10·35					Mean	10·34
99·85	—	10 100	0·02	10·32	10·34						
99·95	—	13 760	−0·36	10·69	10·33						

* Values of H_0 for media of <100% H_2SO_4 are from Hammett and Deyrup, corrected according to Hammett and Paul (*locc. cit.*).

a lower value of ϵ_{ion} at the longer wave-length, but in the absence of further evidence that this is the correct thing to do the experimental figure has been retained. In the case of the *m*-substituted derivatives, H_0 and pK_a suggest that ionisation is a few units % incomplete in the 65% medium; but comparison of results at the two wave-lengths shows that the effect of this is made up for by the exaltation of intensity which is believed to occur.

m-*Nitroaniline Cation.*—As judged from the curves in Fig. 2, the second-stage ionisation must be incomplete in 65% oleum. Because the NH_3^+ group is remarkable for its small influence on ultra-violet spectra, the reference value of ϵ_{ion} is assumed to be the same as that of the phenylnitracidium cation. Support for this is as follows. (1) The values of $\epsilon_{max.}$ of the *m*-nitroaniline cation and (un-ionised) nitrobenzene are very nearly equal in concentrated sulphuric acid as solvent. (2) Several pairs of compounds differing by a *p*-NH_3^+ group have been compared in aqueous solution (Doub and Vandenbelt, *loc. cit.*) and the values of $\epsilon_{max.}$ differ by an average of 1000 units only (the cation always absorbs more strongly). A difference of this magnitude would raise the ionisation ratios by an average of <0·05 unit; moreover, in the *m*-series closer agreement is not improbable.

TABLE 2. *The second ionisation constant of* m-*nitroaniline.*

Medium						Medium					
H_2SO_4, %	SO_3, %	ϵ_{mean} (λ 3200—3250 Å)	log [Base]/[Ion]	$-H_0$	$-pK_a$	H_2SO_4, %	SO_3, %	ϵ_{mean} (λ 3200—3250 Å)	log [Base]/[Ion]	$-H_0$	$-pK_a$
99·0	—	600	—	—	—	105·85	26·0	3 690	0·60	12·61	13·21
102·73	12·1	1 600	1·16	12·10	13·26	107·30	32·4	5 500	0·33	12·80	13·13
104·16	18·5	2 470	0·86	12·37	13·23	114·5	64·5	12 050	−0·46	13·67	13·21
104·22	18·8	2 570	0·83	12·38	13·21			16 000 = ϵ_{ion}			
										Mean	13·21

2 : 4-*Dinitrotoluene* (*Fig.* 1) *and* 2 : 4-*Dinitrochlorobenzene.*—To calculate pK_a and ϵ_{ion}, the ionisation ratio is re-written as

$$[\text{Base}]/[\text{Ion}] = (\epsilon_{ion} - \epsilon)/(\epsilon - \epsilon_{base}) = K_a/h_0 \; ; \; H_0 = -\log_{10} h_0$$

Rearrangement gives $\epsilon_{ion} - \epsilon = K_a\{(\epsilon - \epsilon_{base})/h_0\}$. The factor in { } is tabulated in col. 7, Table 3; K_a, and hence ϵ_{ion}, are evaluated by the method of least squares.

TABLE 3. *Ionisation constant of* 2 : 4-*dinitrotoluene* (3300—3350 Å).

Medium							
H_2SO_4, %	SO_3, %	ϵ_{mean}	$\epsilon - \epsilon_{base}$	$-H_0$	$h_0 \times 10^{-11}$	$\left\{\frac{(\epsilon - \epsilon_{base})}{h_0}\right\} \times 10^{11}$	$-pK_a$
99·0	—	1 700	—	—	—	—	—
101·64	7·3	3 400	1 700	11·86	7·2	236	—
102·74	12·2	4 170	2 470	12·10	12·6	196	—
104·23	18·8	5 870	4 170	12·38	24·0	174	—
105·46	24·3	7 060	5 360	12·56	36·3	152	12·6$_6$
106·07	27·0	7 790	6 090	12·68	47·9	130	—
107·30	32·4	9 220	7 520	12·80	63·1	119	—
114·5	64·5	12 550	10 850	13·67	470	23·1	—
		ϵ_{ion} = 13 900					

s-*Trinitrobenzene and* 2 : 4 : 6-*Trinitrotoluene.*—Some ionisation was apparent in 36% oleum and appreciably more, probably 10—15 and 20—30% respectively, in 65% oleum (Figs. 5 and 6). The conversion was too small for quantitative conclusions to be drawn. Trinitrotoluene is evidently a stronger base than trinitrobenzene.

DISCUSSION

The influence of substituents on the basicity of the nitro-group is shown in Table 4, where the results are expressed in terms of the acidity constant, pK_a, of the arylnitracidium cation. The pK_a's refer to aqueous rather than sulphuric acid solutions for the following reason. In the determination of the H_0 function it is assumed that the ratios f_{base}/f_{ion} (where the *f*'s are activity coefficients relatively to the standard state of a *dilute aqueous solution*) have the same value in a particular medium, excluding media of low dielectric constant, for all bases. Granting this, it follows that the K_a's are thermodynamic dissociation constants, defined by $K_a = a_{H^+}a_B/a_{HB^+}$, the activities referring to the standard state in water. Theoretically, therefore, although the experiments are made in sulphuric

acid media, the activity coefficients allow automatically for the change of solvent and the acidity constants refer to the idealised but unrealisable standard of an ideally dilute solution in water. The assumption involved is supported by the demonstration, in occasional cases, that the acidity constant is independent within experimental error of the solvent used for the determination (Hammett and Deyrup, *loc. cit.*; Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 827); but it should be remarked that this test has not been applied to H_2SO_4–H_2O mixtures more concentrated than 70%.

The absolute value of the pK_a's in Table 4 is of little significance owing to the uncertainty in the H_0 scale. Essentially, the measurements yield *relative* acidity constants (col. 3) and the accuracy here, limited by the irregular physical effects of the medium, is probably better than 0·1 unit.

Acidity Function Scale.—The new measurements furnish values of H_0 which, in oleum, are higher (less negative) than those published by Brand (*loc. cit.*). The difference between the scales is fairly small in dilute oleum but increases with rising oleum strength, and is due entirely to the difficulty of taking the medium effects properly into account. These effects influence particularly the results in the middle range of oleum composition, where H_0 changes slowly with concentration.

TABLE 4. *Influence of substituents on the acidity constant of nitrobenzene.*

Substituent	Acidity constant, $-pK_a$	$\Delta pK = pK_a^\circ - pK_a$ obs.	calc.	Substituent	Acidity constant, $-pK_a$	$\Delta pK = pK_a^\circ - pK_a$ obs.	calc.
p-Bu^t	10·2	−1·1	−0·27	*m*-Cl	12·15	0·89	0·83
p-Me	10·34	−0·92	−0·13	*m*-NO_2,*p*-Me	12·6$_4$	1·4	1·4
m-Me	10·84	−0·42	−0·21	*m*-NO_2	—	—	1·5
H	11·26	0·0	0·0	*m*-NH_3^+	13·2$_1$	1·9$_5$	1·8
p-F	11·50	0·24	0·58	*m*-NO_2,*p*-Cl	13·6	2·3	2·0
p-Cl	11·56	0·30	0·50	3 : 5-di-NO_2,4-Me	and 3 : 5-di-NO_2 : Too weak to be measured.		
m-F	12·15	0·89	0·87				

The variation of H_0 with medium composition is shown in Fig. 8. In this system, disulphuric acid is a weak acid and water a strong base, and the analogy with the pH change on neutralisation in aqueous solution will be obvious; the " neutral " point is at the composition H_2SO_4.

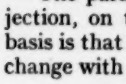
Calculation of Acidity Constants relatively to Nitrobenzene by the Electrostatic Theory.—The method of calculation of the influence of a dipolar substituent on the acidity constant, due to Kirkwood and Westheimer (*J. Chem. Physics*, 1938, **6**, 503, 513; 1939, **7**, 437; *Trans. Faraday Soc.*, 1947, **43**, 77), is a development of the earlier ideas of Bjerrum (*Z. physikal. Chem.*, 1923, **106**, 219) and Eucken (*Z. angew. Chem.*, 1932, **45**, 203). The organic molecule or ion is treated as a uniform cavity of low dielectric constant, surrounded by an isotropic medium with the dielectric constant characteristic of the pure solvent. This expresses the fact that the electrostatic field of the dipole operates both through the body of the acid molecule and through the solvent, but all other forms of interaction with the solvent are neglected. The cavities are idealised, and benzenoid molecules are approximated by an oblate spheroid, generated by rotation of an ellipse about its minor axis, the acid group and the substituent dipole lying on the focal circle (Sarmousakis, *J. Chem. Physics.*, 1944, **12**, 277). The acidity constant relatively to nitrobenzene, *i.e.*, the equilibrium constant of equation (1), where $\log K = \Delta pK$ (Table 4), is given by equation (2).

$$X{\cdot}C_6H_4{\cdot}\overset{+}{N}O{\cdot}OH + C_6H_5{\cdot}NO_2 \overset{K}{\rightleftharpoons} X{\cdot}C_6H_4{\cdot}NO_2 + C_6H_5{\cdot}\overset{+}{N}O{\cdot}OH \quad . \quad (1)$$

$$-2{\cdot}3kT\,.\,\Delta pK = e\mu_\zeta \cos(\mu_\zeta, r)/r\varepsilon_\zeta^2 + e\mu_\phi \cos(\mu_\phi, r)/r\varepsilon_\phi^2 \quad . \quad . \quad . \quad (2)$$

In (2), μ_ζ and μ_ϕ are respectively the components of the substituent dipole, μ, along the radius and tangent of the focal circle, and ε_ζ and ε_ϕ are the corresponding " effective " dielectric constants; r is the length of the line joining the dipole and the acid group, forming the angles (μ_ζ, r) and (μ_ϕ, r) with μ_ζ and μ_ϕ respectively. The standard free-energy change in (1) is assumed to be equal to the net electrostatic work done.

The parameter r is chosen to be the distance from the substituent dipole to the projection, on the symmetry axis, of the oxygen atoms of the nitro-group. The physical basis is that in this way we calculate the sum of the electrostatic energies required to interchange with the unsubstituted system the ionisable proton *and* the $-NO_2$ dipole, the latter represented by (I) (Pauling, "Nature of the Chemical Bond," Cornell Univ. Press, 1945, p. 202). This is different from the case of the carboxylic acids, where the dipole of the $-CO_2H$ group is included by measuring r to the ionisable proton. Actually, the ΔpK's differ considerably in the benzoic acid (Judson and Kilpatrick, *J. Amer. Chem. Soc.*, 1949, **71**, 3115) and the nitrobenzene system, and it is noteworthy that a physically intelligible change of r, other parameters being kept constant, will express the results in both series.



(I)

The other parameters in equation (2) conform to the known structure of the molecules. The substituent dipole was approximated by a point dipole placed at the mid-point of the bond to the aromatic nucleus, except for $-NO_2$ where it was located on the nitrogen atom. The partial distribution of the dipoles over the aromatic nucleus has to be neglected, a weaknesss when the theory is applied to fully conjugated systems. The quantities r and c (the radius of the focal circle) were calculated from the molecular geometry. The size of the cavity, V, is about $1\frac{1}{2}$ times the volume of the solute molecule as estimated from Traube's rule or from the van der Waals radii, and includes an empty shell between the solute and surrounding solvent molecules. The effective dielectric constants, ε_ζ and ε_ϕ, are determined by the dielectric constants of the cavity ($\varepsilon_i = 2{\cdot}0$; Kirkwood and Westheimer, *loc. cit.*) and the solvent ($\varepsilon_{20°} = 80$, it being remembered that the K_a's refer to a standard state in water), and the ratio V/c^3 which defines the location of the point dipole and the nitro-group relatively to the boundary of the cavity. The cavity volumes, bond lengths, and dipoles were as follows:

Substituent, X	F	Cl	CH_3	Bu^t	NO_2	NH_3^+
μ, D	1·57	1·72	0·4	0·7	4·21	—
Bond length, X–Ar (Å)	1·31	1·69	1·50	(1·50)	1·46	(1·46)
Cavity volume, V (Å^3)	260	260	260	310	290	260

For *m*-derivatives the results of the calculation are satisfactory. In other cases the electrostatic theory is, by itself, insufficient. Thus, the poor agreement for *p*-fluoro- and *p*-chloro-nitrobenzene is due to resonance interaction between the substituents; this is already well known from the exaltation of the dipole moment (Groves and Sugden, *J.*, 1937, 1782; Hurdis and Smyth, *J. Amer. Chem. Soc.*, 1942, **64**, 2212). The ΔpK values indicate, in agreement with other evidence, that the resonance energy is greater for *p*-F than for *p*-Cl.

Environmental Factors; Entropy of Ionisation.—The anomalous behaviour of the *p*-alkyl substituents is clearly not due to hyperconjugation alone and is unlikely to have an "electronic" explanation at all. It probably arises from solvent–solute interaction which has been neglected (*i.e.*, assumed constant) hitherto. Variations here, although small, may be of the same order as the electrostatic energy differences. This can be decided from the entropies of ionisation. Using Bjerrum's formula, we have (Hammett, *J. Chem. Physics*, 1936, **4**, 613; Gurney, *ibid.*, 1938, **6**, 499)

$$\Delta S^\circ = \Delta G^\circ \mathrm{d}(\ln \varepsilon)/\mathrm{d}T$$

where ΔS° and ΔG° refer to equilibrium (1). On Sarmousakis's model, only *p*-derivatives being considered, ε is replaced by ε_ζ. On either model, ΔS° and ΔG° must be of opposite sign if the theory is sufficient; otherwise $\mathrm{d}(\ln \varepsilon)/\mathrm{d}T$ is positive, which implies a dielectric constant increasing with temperature. Because the variation of $T\Delta pK$ with T is small, only rough values of $\Delta S^\circ = 2{\cdot}3R\mathrm{d}(\ln T\Delta pK)/\mathrm{d}T$ are available, and to evaluate these it has been necessary to assume that the spectra themselves are independent of temperature (15—45°).

Free energy and entropy of ionisation [Equilibrium (1), 99·8% H_2SO_4].

Substituent	ΔG°_{291}	ΔS°_{291}	$\mathrm{d}(\ln \varepsilon)/\mathrm{d}T$
p-CH_3	+1220	+2·1	+0·001$_7$
p-F	− 320	+0·64	−0·002

The result for *p*-nitrotoluene shows that ΔS°, which should be small and negative, is about 3 or 4 cal. deg.$^{-1}$ mole^{-1} different from the expected value. This must be due to entropy of solvation, and it is then no longer justified to equate ΔG° with the net electrostatic work. In water the values of $d(\ln \varepsilon)/dT$ and $d(\ln \varepsilon_\zeta)/dT = (\varepsilon_\zeta/\varepsilon)(d \ln \varepsilon/dT)$ are −0·005 and −0·0003, respectively. The result for *p*-fluornitrobenzene is quite reasonable; $\Delta S_{solv.}$ must be small, if not zero. However, effects of this kind are responsible for the fact that a plot of pK_a against the σ-constant gives a rather poor approximation to a straight line.

Note on the Kinetics of Nitration of 2 : 4-*Dinitrotoluene in Oleum.*—The velocity of nitration of 2 : 4-dinitrotoluene in oleum (Bennett *et al.*, *J.*, 1947, 474) falls with rising concentration of sulphur trioxide. The explanation originally offered has been shown to be incorrect (Melander, *Arkiv Kemi*, 1950, **2**, 211; Ingold, Hughes, and Reed, *J.*, 1950, 2400), and it is now clear that part, at least, of the decline in velocity must be due to protonation of the dinitrotoluene, the ions produced being almost totally unreactive (Brand and Paton, *J.*, 1952, 281). It is not yet possible to allow quantitatively for the influence of the equilibrium on the kinetics, because the ionisation data refer to 18° and the rate measurements to 90°; but as they stand the changes are almost equal and opposite. The real dependence of nitration velocity on medium composition in oleum must be quite small.

The Second Ionisation Constant of m-*Nitroaniline.*—The pK_a value in Table 4 was evaluated by using the H_0 scale, a step which is equivalent to assuming that the dipolar positive ion m-$H_3\overset{+}{N}\cdot C_6H_4\cdot\overset{+}{N}O\cdot OH$ behaves in the same way as a univalent electrolyte. In aqueous solution this is permissible at high ionic strengths (Bjerrum, *Z. physikal. Chem.*, 1923, **104**, 147; Güntelberg and Schöidt, *ibid.*, 1938, **135**, 393; cf. Fuoss and Edelson, *J. Amer. Chem. Soc.*, 1951, **73**, 269; Fuoss and Chu, *ibid.*, p. 949), but whether it applies in oleum media is hypothetical. However, it is possible to estimate $H_0 - H_+$, where H_+ relates to a bivalent cation with spherical symmetry of charge, and thus to decide whether in a real case it will be serious if this quantity is neglected. The method of calculation was suggested to us by Dr. V. Gold. From the definition of the acidity function

$$H = -\log (f_B \cdot a_{H^+}/f_{HB^+}); \quad H_+ = -\log (f_{B^+} \cdot a_{H^+}/f_{HB^{++}})$$

we have

$$H_0 - H_+ = \log (f_B \cdot f_{HB^+}/f_{HB^{++}} \cdot f_B) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Referred to the standard state in water (dielectric constant ε_0), and it being assumed that the free energy of transfer of an ion is equal to the electrostatic potential energy difference, the ionic activity coefficient f_i, in pure, anhydrous sulphuric acid (dielectric constant ε) is given by equation (4) (Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold, 1943, Chap. 3),

$$\ln f_i = (z_i e)^2 \left\{\frac{1}{\varepsilon} - \frac{1}{\varepsilon_0}\right\} \Big/ 2kTr \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where z_i is the valency and r the radius of the ion, the charge distribution being supposed spherical. By using equation (4) to calculate f_{B^+}, f_{HB^+}, and $f_{HB^{++}}$ [only ratios of the f's occur in equation (4), which helps to take non-electrostatic factors into account], and assuming that the radii of B, HB^+, B^+, and HB^{++} are all equal, we obtain from (3) ($f_i \longrightarrow 1$ as $\varepsilon \longrightarrow \varepsilon_0$)

$$H_0 - H_+ = -e^2 \left\{\frac{1}{\varepsilon} - \frac{1}{\varepsilon_0}\right\} \Big/ 2{\cdot}3kTr$$

(It may be noted that, with the same conventions, $H_+ + H_- = 2H_0$.) Introducing the values $\varepsilon_0 = 80$, $\varepsilon \sim 125$ (unpublished measurements, with Drs. James and Rutherford) and $r = 4$ Å we have from this equation

$$H_+ = H_0 - 0{\cdot}28 = -11{\cdot}2 \ (100{\cdot}0\%\ H_2SO_4)$$

This result agrees in sign with Michaelis and Granick's observation (*J. Amer. Chem. Soc.*, 1942, **64**, 1861) that an acidity scale established partly with multipolar bases in *aqueous* sulphuric acid is a few tenths of a unit more negative than Hammett's H_0, but it is doubtful

if the difference really exceeds the experimental error. The increment of 0·28 unit would be an appreciable, but small, correction to the ΔpK of *m*-nitroaniline. However, bearing in mind that it refers to an ideal, spherically symmetrical cation and exaggerates the difference for ions of lower symmetry, we conclude that the correction can be dropped without serious error.

The value of ΔpK in Table 4, col. 8, is calculated from the equation (Sarmousakis, *loc. cit.*)

$$2{\cdot}3\,kT\,.\,\Delta pK = e^2/r\varepsilon_E$$

in which the symbols have the same meaning as in equation (2), and the parameters r and ε_E are evaluated by similar conventions.

Comparison with Cryoscopic Results.—These measurements (Gillespie, *loc. cit.*) are expressed as basic dissociation constants, $K_b = [Ar\cdot\overset{+}{N}O\cdot OH][SO_4H^-]/[Ar\cdot NO_2]$, brackets referring to concentrations. The equality being granted of the former ratios f_B/f_{HB^+} (here the f's are relative to the standard state in water) in a single medium, $\log(K_b^\circ/K_b)$ has the same thermodynamic significance as ΔpK in Table 4. As shown below, the basicities are in the same order but the quantitative agreement is poor; nor is this due to the temperature differences, the effect of which is trivial.

Base	*p*-$C_7H_7\cdot NO_2$	$C_6H_5\cdot NO_2$	*m*-$H_3\overset{+}{N}\cdot C_6H_4\cdot NO_2$	$C_7H_5(NO_2)_3$
$\log(K_b^\circ/K_b)$, 9°	−0·84	(0·0)	0·31	0·63
ΔpK, 18°	−0·92	(0·0)	$1{\cdot}9_5$	~3

An alternative method of comparison is to convert the spectrometric results into ν-factors (Table 5). It is then apparent that the cryoscopic figures are higher than ours (the concentration differences would have the opposite influence), and possible reasons for this are discussed below. For the calculation of K_b, the part of the ν-factor which matters is $\nu - 1$, or $\nu - 2$ in the case of *m*-nitroaniline, and it is noticeable that the best agreement is with *p*-nitrotoluene, where $\nu - 1$ is comparatively large.

It is interesting to examine the cases of trinitrotoluene and the *m*-nitroaniline cation more closely. In neither case is there any spectral evidence of ionisation at the nitro-

TABLE 5. *Number of ions produced per mole of solute (ν-factor): comparison of cryoscopic and spectrometric evidence.*

	Medium			ν-Factor from:	
Solute	H_2O, molality	H_2SO_4, %	$-H_0$	f. p. (0·1M)	Spectrum (10^{-2}—10^{-4}M)
p-$Me\cdot C_6H_4\cdot NO_2$	0·061	99·89	$10{\cdot}4_5$	1·63 *	1·56
$C_6H_5\cdot NO_2$	0·059	99·89	$10{\cdot}4_5$	1·26	1·13
m-$H_3\overset{+}{N}\cdot C_6H_4\cdot NO_2$	0·052	99·91	10·6	2·10	$2{\cdot}0_0$
$C_7H_5(NO_2)_3$	0·074	99·87	10·4	1·09	$1{\cdot}0_0$

* Small variation with concentration.

group in anhydrous sulphuric acid, the limit of detection being about 0·5 g.-ion %. The degree of ionisation of these bases is much less than the analysis of the cryoscopic data indicates, and part of the difficulty appears to be that the calculation of ν-factors from the freezing-points involves assumptions of considerable weight. First, the solutions are assumed to be ideal. Secondly, all solutes are assumed to be solvated; therefore, in spite of (1), the activity or osmotic coefficients may differ from unity unless the molalities are calculated with respect to the "free" solvent. Thirdly, solutions of electrolytes (*e.g.*, *m*-$H_3\overset{+}{N}\cdot C_6H_4\cdot NO_2,SO_4H^-$) are assumed to require a correction for the influence of the SO_4H^- ions on the dissociation of water (equilibrium 5) and the autoprotolysis of the solvent (equilibrium 6). Three parameters are introduced in this way, and the effect of certain adjustments of these is now shown in Table 6. For example, in the case of the

$$H_2O + 2H_2SO_4 \rightleftharpoons H_3O^+ + SO_4H^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$H_2SO_4 + H_2SO_4 \rightleftharpoons H_3SO_4^+ + SO_4H^- \quad . \quad . \quad . \quad . \quad . \quad (6)$$

m-nitroaniline cation, if the correction for the effect of the SO_4H^- ions on (5) and (6) is dropped, the ν-factor falls from 2·10 to 2·00 (col. 11 and 12); the direct question of whether this compound is basic or non-basic, apart from the calculation of K_b which is a question of degree, depends entirely upon a correction to the freezing point. In fact it is basic, but the basicity is only apparent at much higher acidities.

TABLE 6. *Freezing points of trinitrotoluene and* m-*nitroaniline in* H_2SO_4 (Gillespie, *loc. cit.*).*

Molality of			ν-Factor				Molality of			ν-Factor	
			Solvation no. of					*m*-Nitro-			
H_2O	T.N.T.	F. p.	0 †	1	3	4	H_2O	aniline	F. p.	corr.	uncorr.
0·074	—	9·691°	—	—	—	—	0·052	—	9·959°	—	—
,,	0·0222	9·544	1·12	1·09	1·06	1·04	,,	0·01045	9·834	2·08	1·98
,,	0·0385	9·437	1·12	1·09	1·05	1·03	,,	0·02536	9·654	2·11	1·99
,,	0·0537	9·337	1·12	1·09	1·04	1·02	,,	0·03191	9·569	2·10	2·02
,,	0·0721	9·215	1·12	1·09	1·04	1·02	,,	0·03712	9·509	2·10	2·02
,,	0·0963	9·064	1·11	1·07	1·02	1·00					

$k_f = 5·98$ (deg. mole^{-1} kg.).

* The reaction of sulphuric acid with water is written as $H_2O + 2H_2SO_4 \rightleftharpoons H_3O^+,H_2SO_4 + SO_4H^-$, except in the column marked † where solvation of the H_3O^+ ion is omitted. The terms "corrected" and "uncorrected" refer to the supposed mass-action effect of the SO_4H^- ions upon the equilibria (5) and (6).

Although the suggestion that trinitrotoluene ionises to *ca.* 10% in anhydrous sulphuric acid is mistaken, there are nevertheless real differences between the cryoscopy of trinitrotoluene and sulphuryl chloride (Gillespie, Hughes, and Ingold, *J.*, 1950, 2473). The convention being retained that sulphuryl chloride is a perfect non-electrolyte, the experimental result is that the osmotic coefficient of a dilute solution of trinitrotoluene is about 1·12, solvation being disregarded. If we wish at all costs to preserve the assumption that the solutions are ideal, $g - 1$ must represent the solvation correction, and this is achieved if the solvation number is 4 or 5 (Table 6). Since there are three nitro-groups this is not impossible. However, from thermodynamics alone we can determine g or i or f, *but not* ν; and until the nature of the solutions is better understood small differences of ν from an integer must be interpreted with reserve.

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THE UNIVERSITY, GLASGOW, W.2. [*Received, December 3rd*, 1951.]

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253. *Isotopic Tracer Studies of Pyrolytic Reactions. Part I. The Formation of Acetaldehyde.*

By J. BELL and R. I. REED.

The formation of acetaldehyde by the pyrolysis of a mixture of barium acetate and barium formate has been investigated by using an isotopic-tracer technique. It has been found that the ^{13}C content of the carbonyl-carbon atom of the acetaldehyde is approximately normal when the experiments are conducted with barium acetate having an enhanced concentration of ^{13}C in the carboxyl group. This requires the fission of the carbon–carbon bond in the acetate, and a free-radical mechanism has been suggested which is consistent with these observations.

IN describing the preparation of *n*-butyl methyl ketone by the distillation of a mixture of sodium acetate and potassium valerate, Williamson (*J.*, 1852, **4**, 228) predicted the formation of an aldehyde in the case where one of the salts used was a formate. This prediction was confirmed by Limpricht and Ritter (*Annalen*, 1856, **97**, 368), who obtained acetaldehyde from a mixture of calcium acetate and calcium formate. By similar methods Piria (*ibid.*, 1856, **100**, 104) prepared benzaldehyde and cinnamaldehyde.

The appearance of reduction products in such reactions has been reported. Thus the pyrolysis of calcium formate has been shown to yield methyl alcohol by Friedel and Silva (*Bull. Soc. chim.*, 1873, **19**, 481; *Compt. rend.*, 1873, **76**, 1545), and independently by Lieben and Paterno (*Gazzetta*, 1873, **3**, 290). Pagliani (*Ber.*, 1887, **10**, 2055; *Gazzetta*, 1878, **8**, 1) has reported the formation of ethyl alcohol as well as acetaldehyde in the products of salt pyrolysis, and in the reaction between calcium butyrate and calcium formate he obtained dipropylcarbinol and butyl alcohol as well as dipropyl ketone and propaldehyde. He also observed that the pyrolysis of calcium butyrate produced none of the carbinol but only the ketone. Further examination of the pyrolytic decomposition of calcium butyrate showed that the product consisted of a mixture of aldehydes and ketones [Soc. Lefranc et Cie., Can. P. 257 435 (1926); B.P. 216 120 (1923); U.S.P. 1 656 488 (1929); *Chem. Abs.*, 1925, **19**, 77; 1926, **20**, 2332; 1928, **22**, 965; Dépasse, *Bull. Assoc. chim. Sucr. Inst.*, 1926, **43**, 409; *Chem. Abs.*, 1927, **21**, 296; Barbiaglia and Gucci, *Ber.*, 1880, **13**, 1572; Glücksmann, *Monatsh.*, 1895, **16**, 897; Dilthey, *Ber.*, 1901, **34**, 2115].

Kenner and Morton (*Ber.*, 1939, **72**, 452) showed that lead salts of many acids decomposed at lower temperatures than the corresponding calcium salts, frequently giving a better yield of the ketone. In these studies, evidence was obtained of the accumulation in the reaction mixture of a complex which on vigorous heating gave rise to a tar. Treatment of the residue containing the complex with formic acid, however, liberated a further quantity of ketone. A theory analogous to that of the Grignard reaction was suggested to account for the behaviour of lead salts on pyrolysis.

Neunhoffer and Paschke (*Ber.*, 1939, **72**, 919) proposed a mechanism similar to the aceto-acetic ester condensation for the pyrolysis of the salts of dicarboxylic acids in which it was claimed that the reaction proceeded only when an α-hydrogen atom was available for the enolisation which was regarded as the first step in the reaction sequence. This theory was not applied to the pyrolysis of the salts of monocarboxylic acids. A detailed study of the products of the catalytic decomposition of *iso*butyric acid vapour on thoria by Cook, Miller, and Whitmore (*J. Amer. Chem. Soc.*, 1950, **72**, 2732) has been suggested by Brown (*Quart. Reviews*, 1951, **5**, 146) to support the view that reactions of this type proceed by means of free radicals.

In a review of the conditions for the pyrolysis of isotopically labelled barium acetate, Calvin, Heidelberger, Reid, Tolbert, and Yankwich ("Isotopic Carbon," 1949, John Wiley and Sons Inc., New York, p. 249) recorded that the best procedure involved sweeping out the reaction vessel with nitrogen in preference to the vacuum-distillation method. It was observed that methyl-labelled acetate on pyrolysis at 525° left about 3·5% of the methyl-carbon in the carbonate residue whereas 15% remained if the pyrolysis was carried out at 450°. Using carboxyl-labelled acetate it was shown that no carboxyl-carbon appeared in the iodoform obtained by the hypoiodite reaction on the acetone formed.

In a preliminary note (Bell and Reed, *Nature*, 1950, **165**, 402) on the use of the isotopic-tracer technique in the formation of acetaldehyde by pyrolysis, it was shown that the

TABLE 1.

			Concentration (%) of ^{13}C						
					Residual $BaCO_3$:		Carbonyl-carbon atom		
Expt. no.	Temp. (1)	Acetate / Formate (mol. ratio) (2)	Carbonyl-carbon of $Ba(OAc)_2$ (3)	Carbonyl-carbon of pyrolysis mixture (4)	found (5)	calc.* (6)	CH_2O (7)	CMe·CHO (8)	$COMe_2$ (9)
1	650°	0·2	5·45	1·85	2·19	2·18	—	0·98 †	—
2	,,	0·2	2·58	1·36	1·54	1·43	—	1·08	—
3	,,	0·5	4·03	2·09	2·43	2·20	—	—	—
4	,,	1·0	2·97	2·05	2·31	2·22	—	0·99 †	2·18
5	480	0·2	1·45	1·17	1·20	1·20	—	1·11	1·16
6	,,	0·5	1·41	1·21	1·27	1·26	1·14	1·13	1·39

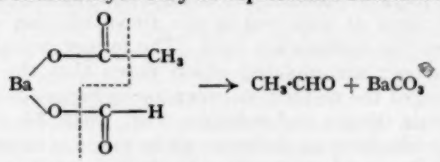
* These values were calculated from the quantity of acetaldehyde produced (determined by titration as acetic acid), on the assumption that the carbonyl groups of the acetaldehyde and formaldehyde had a normal ^{13}C value, whereas that of the acetone had the same enrichment as the carboxyl-carbon atom of the barium acetate.

† Converted into *p*-nitrobenzyl acetate for combustion.

aldehyde obtained from barium acetate enriched with ^{13}C in the carboxyl group had an approximately normal isotopic enrichment value. A fuller examination of this reaction has now been carried out. In these experiments the pyrolysis of mixtures of barium acetate and barium formate yielded a mixture of volatile products, a residue of barium carbonate, and a small quantity of tar. A small volume of gas in which carbon dioxide has been detected was also produced. The volatile products consisted principally of a mixture of acetaldehyde and acetone, together with some formaldehyde and, possibly, alcohols formed by the reduction of these. No attempt was made to detect or separate any of the derived alcohols, and the method of isolation of the acetaldehyde present, that of selective oxidation, was not invalidated by their presence. The results, shown in Table I, have confirmed the fact that, where the concentration of ^{13}C in the carboxyl group of the acetate was enhanced, the isotopic ratio for the carbonyl-carbon atom of the acetaldehyde formed was approximately normal.

The enrichment of the barium carbonate residue is shown by a comparison of columns (4) and (5).

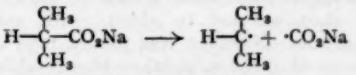
The formation of the acetaldehyde may be represented schematically as follows :



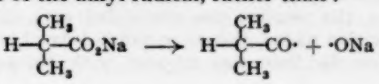
The observation that the acetaldehyde has an approximately normal ^{13}C content is clearly inconsistent with the theory that the acetaldehyde was formed by reduction of the acetate, the formate having acted as a reducing agent. Such a hypothesis would require that the carbonyl-carbon atom should have an enhanced concentration of ^{13}C, having been derived from the enriched carboxyl-carbon atom of the acetate. Moreover, as the above scheme shows, the formation of "normal" acetaldehyde must be accompanied by a separation of the methyl group from the carboxyl group.

Experiments with non-isotopic materials showed that the decomposition of barium acetate proceeded rapidly only at temperatures above 440°. In the pyrolysis of calcium acetate Ardagh, Barbour, McClellan, and McBride (*Ind. Eng. Chem.*, 1924, **16**, 1133) reported that this reaction only became rapid at temperatures around 430° although small traces of acetone were formed at temperatures as low as 160°. The high temperatures required for rapid reaction are consistent with the formation of free radicals and it is suggested that the high-temperature reaction proceeds by a chain mechanism. Such a mechanism in order to be consistent with the isotopic distribution amongst the products, must be initiated either by the formation of free methyl radicals, or by free formyl radicals. It is considered that the reaction is initiated by the free methyl radical, a view favoured by the following observations.

Cook, Miller, and Whitmore (*J. Amer. Chem. Soc.*, 1950, **72**, 2732) have reported the formation of a small quantity of *n*-propyl *iso*propyl ketone, in addition to the expected di*iso*propyl ketone, formed by passing *iso*butyric acid vapour over heated thoria. O'Neill and Reed (unpublished observations) have shown that pyrolysis of sodium *iso*butyrate, a compound which decomposes about 400°, yielded a substantial quantity of both di-*n*-propyl ketone and *n*-propyl *iso*propyl ketone as well as the expected di*iso*propyl ketone. These results can most readily be interpreted by assuming that the rearrangement occurred in an intermediate radical, and it is considered that this evidence favours the process :



followed by rearrangement of the alkyl radical, rather than :



in which the alkyl group which undergoes rearrangement does not contain the electron-deficient centre.

A chain mechanism which is in general agreement with these results is as follows:

Chain initiation: $CH_3{\cdot}CO_2ba \longrightarrow CH_3{\cdot} + {\cdot}CO_2ba$ (ba = ½Ba)

Aldehyde formation: $CH_3{\cdot} + H{\cdot}CO_2ba \longrightarrow CH_3{\cdot}CHO + {\cdot}Oba$

Acetone formation: $CH_3{\cdot} + CH_3{\cdot}CO_2ba \longrightarrow CH_3{\cdot}CO{\cdot}CH_3 + {\cdot}Oba$

Chain continuation: $CH_3{\cdot}CO_2ba + {\cdot}Oba \longrightarrow CH_3{\cdot} + ba_2CO_3$

Chain termination: $2CH_3{\cdot} \longrightarrow C_2H_6$ or $CH_4 + CH_2$: etc.

$2\ {\cdot}Oba \longrightarrow (Oba)_2$

${\cdot}CO_2ba + {\cdot}Oba \longrightarrow ba_2CO_3$

The relative importance of the methods of chain termination cannot be decided by the present experimental method and the above reactions have been listed as probable processes which are consonant with the remainder of the proposed mechanism.

The function of the metal is obscure, and there is no evidence to decide whether the salt reacts in the covalent form as indicated in the above reaction scheme, or whether the reaction occurs between the carboxylate ions. The former postulate is preferred as considerable evidence has been accumulated which shows that the yield of acetone varies markedly with variation of the metal even when such changes are restricted to the alkali and alkaline-earth metals (Rojan and Schulten, *Ber.*, 1926, **59**, 499; Kronig, *Z. angew. Chem.*, 1924, **37**, 667). Similarly no decision can be made as to the mode of formation of formaldehyde, its reduction, or decomposition products, except in so far as the high temperatures employed are again consistent with a mechanism involving homolytic fission.

Examination of the isotopic values for the carbonyl-carbon atom of the acetaldehyde shows that the value for the ^{13}C abundance is slightly lower than the usual value of 1·12%. This may be connected with the "isotope effect" (Roe and Hellmann, *J. Chem. Phys.*, 1951, **19**, 660) in which at least at moderate temperatures the fission of a ^{12}C–^{12}C bond is appreciably favoured with respect to that of a ^{12}C–^{14}C bond. The value for the ratio of relative frequencies of fission of the two types of bond apparently depends to some extent on the reaction involved, and the usual value at room temperature is about 1·05, so that at the high temperatures used in the present experiments, where the ^{12}C–^{13}C bond is concerned, the "isotope effect" is probably negligible. Recent work by Evans and Huston (*ibid.*, 1951, **19**, 1214) suggests that the effect may, however, be operative in the combustions.

As a result of the simple theory proposed the carbonyl-carbon atom of the acetone should have the same ^{13}C content as the original acetate. The measured values for experiments (4) and (6) are of the order of magnitude expected, and the deviations are within the probable experimental error. In experiment (5), where the acetate/formate ratio is smaller, the probable error is larger since a disadvantage of the method of selective oxidation used to isolate the acetaldehyde is its failure to cause complete conversion into acetic acid. A consequence of this is that any aldehyde left unoxidised by the chromic acid appears finally along with the acetone as acetic acid.

Experimental

Synthesis of Carboxyl-labelled Barium Acetate.—Carboxyl-labelled barium acetate was prepared by a method substantially the same as that recorded by Calvin *et al.* (*op. cit.*, p. 178). ^{13}C-Enriched carbon dioxide, prepared by treating enriched barium carbonate with an excess of concentrated sulphuric acid, was distilled on to a calculated quantity of previously prepared methylmagnesium iodide frozen in liquid nitrogen in a high-vacuum system. The mixture was then warmed to about −15° and agitated to facilitate the absorption of the carbon dioxide. Nitrogen was passed into the system, and the reaction vessel removed. A small excess of dilute sulphuric acid was added to decompose the Grignard reagent, the solution neutralised with sodium hydroxide solution, and the ether removed by evaporation. After cooling, the solution was reacidified with dilute sulphuric acid, and an excess of silver sulphate solution added, the silver iodide formed being filtered off and the acid filtrate steam-distilled. The distillate was titrated with barium hydroxide solution, and

evaporated to dryness. The yield of barium acetate, determined by titration and weighing the residue on evaporation, varied from 68—90%.

Pyrolysis.—Weighed quantities of isotopically enriched barium acetate and normal barium formate were mixed, dissolved in a small quantity of water, and evaporated to dryness on a water-bath, and the mixed salt was heated at 120° for several hours. The dried mixture was finely powdered and a known weight, usually 200—400 mg., used in each pyrolysis.

The pyrolyses were carried out as follows. The salt mixture, in a silica boat, was placed in a silica tube 20 cm. long and 1 cm. in diameter. The outlet of the tube was connected by means of standard ground joints to two spiral traps in series immersed in liquid nitrogen, and then to a bubbler containing saturated aqueous dimedone solution. The tube was heated by means of a manually controlled electric furnace. The furnace, constructed in two sections, was brought to the required temperature and then placed in position around the silica tube. During the pyrolysis the whole apparatus was swept out by a stream of nitrogen previously passed over copper turnings at red heat, then through a glass spiral to allow the gas to cool, and finally through phosphoric oxide. The volatile products were swept into the spiral traps in which they condensed, the gases passing through the bubbler. The bubbler enabled the rate of flow of the nitrogen to be determined, this rate having been shown to have an important effect on the yield (Ardagh, Barbour, McClellan, and McBride, *loc. cit.*). The dimedone solution also made it possible to determine whether or not any aldehyde passed through the spiral traps. It was found that if the rate of flow was greatly in excess of 2 l. per hour a considerable quantity of the dimedone–aldehyde adduct was obtained. In cases where the rate of nitrogen flow was at or slightly below this figure, the precipitate was slight and as far as could be determined by m. p. and mixed m. p. determinations was the formaldehyde–dimedone derivative.

In several reactions a small quantity of tar condensed on the cooler parts of the reaction tube and did not reach the spiral traps. The bulk of this deposit was ether-soluble. In one case it was assayed for the ^{13}C content and found to be slightly enriched.

The contents of the traps were allowed to warm to about 0°, there being then in most cases a slight evolution of gas. This gas was shown in two non-isotopic experiments to be carbon dioxide, giving a turbidity with lime water.

The liquid contents of the tube were washed out with a known volume of water and oxidised by a chromic acid mixture.

Oxidation.—The principal products of the pyrolyses were acetaldehyde and acetone, and possibly the reduction products ethyl and propyl alcohol respectively. The method of analysis was required to provide a pure sample of the acetaldehyde or the ethyl alcohol, or a product derived from one of these, not contaminated with acetone or with any products from the formaldehyde. The method of selective oxidation was chosen which had the advantage that the ethyl alcohol and the acetaldehyde were both oxidised to the same product, acetic acid, which could be determined by titration and the salt so formed easily recovered for isotopic analysis. The method adopted was that of Adams and Nicholls (*Analyst*, 1929, **54**, 2; Nicholls, "The Determination of Alcohol," Tatlock Memorial Lecture, Royal Institute of Chemistry, 1948), whereby the formaldehyde or methyl alcohol would be oxidised to carbon dioxide and water, and the acetaldehyde or its reduction product to acetic acid. Any *iso*propyl alcohol formed would be oxidised to acetone whereas acetone would be unaffected. As the authors indicated, the method is not quantitative on a semi-micro-scale, and a short investigation was carried out to determine the discrepancies which would occur with such quantities as might be expected from the pyrolyses. The oxidations were carried out under the conditions recommended by the authors, as preliminary experiments showed that either increasing the strength of the oxidising mixture or lengthening the time of reaction caused a significant oxidation of the acetone.

Experiments were carried out with pure samples of methyl alcohol, ethyl alcohol, acetone, and acetic acid, each being treated separately in order to find the extent of oxidation and the loss on distillation. About 250 c.c. of the distillate were collected and titrated with carbonate-free sodium hydroxide.

The method, as shown by the results in Table 2, does not give a quantitative yield of acetic acid, and in the results listed in the discussion, the estimated yields of acetaldehyde have been corrected for this by means of an empirical multiplying factor obtained from the data described below. Another aspect to be considered was that the methyl alcohol was not oxidised quantitatively to carbon dioxide and water, and thus the acetic acid would be contaminated by formic acid. The latter acid was removed by the following procedure (Fouchet, *Bull. Soc. chim.*, 1912, **11**, 325). After titration, the solution of the sodium salts was evaporated to dryness, the residue heated with alkaline permanganate on a water-bath for 30 minutes, allowed to cool, and

acidified with dilute sulphuric acid. Excess of ferrous sulphate solution was then added to destroy the permanganate, the solution refluxed to remove carbon dioxide, and steam-distilled as in the previous oxidation by chromic acid. About 250 c.c. of the distillate were collected, and again titrated with carbonate-free sodium hydroxide solution. The results of this treatment are tabulated in the last two columns of Table 2.

TABLE 2. *Efficiency of oxidations.*

		Oxidation by CrO_3			Subsequent oxidation by $KMnO_4$	
			Yield of acid,			
Substance	Amount mmole	Titre, ml.	mmol.†	%	Titre, ml.‡	Yield, %
Titration blank	—	0·49	—	—	—	—
Acetic acid	0·119	5·17	0·114	95·8 *	—	—
	0·457	18·90	0·447	97·8		
Acetone	0·280	0·58	0·0002	0·07	—	—
	0·310	0·58	0·0002	0·07	—	—
	0·381	0·67	0·0004	0·14	—	—
Ethyl alcohol	0·104	4·34	0·0967	93·6	—	—
	0·448	16·40	0·399	86·2	—	—
	0·783	30·59	0·755	93·3	—	—
	0·794	28·88	0·712	86·8	—	—
	0·832	30·61	0·756	90·8	—	—
Methyl alcohol	0·144	1·71	0·0305	21·2	—	—
	0·156	1·84	0·0339	21·7	—	—
	0·175	1·81	0·0331	18·9	—	—
	0·203	2·23	0·0436	21·5	—	—
	0·297	4·44	0·0992	33·4	0·45	nil
	0·586	11·54	0·277	47·2	1·65	4·96
	0·818	23·05	0·566	69·2	1·68	3·57

* Distillation loss, 3·3%.
† Yield of acid is corrected for titration blank, and loss of acetic acid in steam distillation.
‡ Titre for distillate after permanganate oxidation is corrected both for titration blank and for loss of acetic acid in steam-distillation.

A series of experiments was also carried out involving known mixtures of ethyl and methyl alcohols and acetone; the results are shown in Table 3. Each mixture was oxidised by the chromic acid method, steam-distilled, and titrated. The titrated solution was then distilled, the first 60 c.c. of distillate, which contained the acetone, being collected and reserved for further treatment. The residue was dried on a water-bath and heated with alkaline permanganate, treated as described above, and steam-distilled. This distillate contained the acetic acid which was then determined by titration. The neutralised solution was evaporated to dryness, and the resulting sodium acetate recrystallised from aqueous alcohol and retained for subsequent isotopic assay.

20 C.c. of sodium hydroxide solution were added to the distillate containing the acetone followed by 20 c.c. of N-iodine. The mixture was set aside for about 15 minutes and the iodoform extracted with ether. The solution was evaporated to small bulk, allowed to cool, and acidified with dilute sulphuric acid. Excess of silver sulphate was then added and the silver iodide formed filtered off. The filtrate was steam-distilled and the distillate, about 250 c.c., titrated with carbonate-free sodium hydroxide solution. In the case of isotopically enriched samples, the neutralised solution was evaporated to dryness, and the sodium acetate recrystallised from aqueous alcohol.

TABLE 3.

Acetone, mmol.	Methyl alcohol, mmol.	Ethyl alcohol, mmol.	Titre after $KMnO_4$, oxidation, ml.	Yield (by titration), mmol.*	Yield of EtOH as AcOH, %
0·302	0·541	0·175	7·07	0·171	97·9
0·165	0·821	0·198	7·47	0·181	91·5
0·368	0·432	0·225	7·80	0·190	84·6
0·423	0·651	0·323	10·70	0·284	87·9
0·433	0·351	0·493	17·54	0·443	89·9

* The yield is corrected for two steam-distillations and the titration blank.

An average value for the extent of the oxidation of the ethyl alcohol in these mixtures is 90·4%, and accordingly the observed titration values in the isotopic experiments were multiplied by a factor of 1·11 to give the probable quantity of acetaldehyde formed, and provide a rough value for calculation of the theoretical enrichment of the barium carbonate on the basis of the suggested mechanism. It should be noted that when the acetone and ethyl alcohol were present in nearly equal amounts, a condition frequently fulfilled in the pyrolyses, the oxidation determined by titration was close to 90·4%, so that the errors involved in these experiments were not large.

Isotopic Assay.—The combustions were carried out directly on the sodium acetate, with two exceptions in which the salt was converted into *p*-nitrobenzyl acetate. This ester was prepared by heating *p*-nitrobenzyl bromide with the sodium acetate in ethyl alcohol under reflux for about 2 hours. The mixture was evaporated to dryness and dissolved in a small quantity of light petroleum. The ester was separated from the unchanged bromide by passing this solution down a small alumina column and eluting it with light petroleum–benzene, the unchanged bromide remaining strongly absorbed at the top of the column.

All samples assayed were converted into carbon dioxide by the " wet combustion method " of van Slyke and Folch (*J. Biol. Chem.*, 1940, **136**, 509) in the type of apparatus described by Weinhouse (" Preparation and Measurement of Isotopic Tracers," Edwards, Ann Arbor, Michigan, 1946, p. 43).

The carbon dioxide samples so obtained were assayed (in part) on a Metropolitan-Vickers Ltd. Mass Spectrometer, Type M.S.2. The abundance ratio being determined from the intensities of the peaks of mass numbers 44 and 45.

Materials.—Diethyl ether. A B.D.H. sample was dried ($CaCl_2$, P_2O_5, Na wire). Samples required for Grignard reactions were distilled immediately before use.

Acetone. B.D.H. acetone was refluxed for some hours with potassium permanganate, dried (Na_2SO_4), and distilled. A sample of this was then treated with sodium iodide, and the complex formed separated by filtration and decomposed by distillation, giving material of b. p. 56°/760 mm.

Ethyl alcohol. " Absolute " alcohol was dried by Smith's method (*J.*, 1927, 1288) as modified by Manske (*J. Amer. Chem. Soc.*, 1931, **53**, 1106). A sample of b. p. 78·4° was collected.

Methyl alcohol. This was dried by refluxing it with magnesium turnings, and then distilling it. The fraction of b. p. 65°/765 mm. was collected.

Methyl iodide. This was shaken with 10% sodium carbonate, water, sodium thiosulphate solution, and finally water, dried (P_2O_5), and distilled. A fraction of b. p. 41°/734 mm. was collected.

p-*Nitrobenzyl bromide.* A B.D.H. sample, recrystallised from aqueous alcohol and dried ($CaCl_2$), had m. p. 99°.

Barium formate. A sample of 70% formic acid was steam-distilled and neutralised with aqueous barium hydroxide. The crystals formed by evaporation of this solution were twice recrystallised from small quantities of water.

Inorganic materials. These were of " AnalaR " standard where possible.

Grateful acknowledgment is made of gifts of isotopically enriched barium carbonate from the Houdry Process Corporation and the Atomic Energy Research Establishment, Harwell, and for a grant from the Department of Scientific and Industrial Research for the purchase of the mass spectrometer.

UNIVERSITY OF GLASGOW. [*Received, December 6th*, 1951.]

254. *The Liquid Dinitrogen Tetroxide Solvent System. Part XI.* Compound Formation and Ionic Species in Solutions of Diethylnitrosamine in Liquid Dinitrogen Tetroxide.*

By C. C. Addison and C. P. Conduit.

The physical and chemical properties of solutions of diethylnitrosamine in liquid dinitrogen tetroxide are interpreted on the basis of the equilibria

$$N_2O_4 + 2Et_2N{\cdot}NO \rightleftharpoons N_2O_4{,}2Et_2N{\cdot}NO \rightleftharpoons (Et_2N{\cdot}NO)_2NO^+ + NO_3^-$$

Electrical conductivity and viscosity measurements, over the temperature range −33° to +16°, show that only the 1 : 2-compound is formed, and that the only effect of temperature change is to adjust the position of the equilibrium. The nature of the cation is deduced from colorimetric measurements and absorption spectra. Anodic oxidation of diethylnitrosamine during electrolysis of these solutions is related to the reaction of dinitrogen pentoxide, and of nitronium pyrosulphate, with diethylnitrosamine. A method for the determination of the latter is described.

Thermal and conductometric measurements, described in Part VI (*J.*, 1951, 1303), showed that the equilibria in mixtures of diethylnitrosamine and liquid dinitrogen tetroxide may be represented as follows:

$$N_2O_4 + nEt_2N{\cdot}NO \rightleftharpoons N_2O_4{,}nEt_2N{\cdot}NO \rightleftharpoons \text{ionic dissociation products} \quad (A)$$

Freezing-point data indicated the existence of the compound $N_2O_4{,}2Et_2N{\cdot}NO$ (m. p. −37·5°) only, but heat-evolution curves suggested that at higher temperatures compounds involving other molecular ratios might exist. If such a variation occurred, there should be a corresponding shift with temperature, in the composition of the mixture at which electrical conductivity was a maximum. In order to compare the results at different temperatures, it was necessary to correct for the changing viscosity of the solutions. The viscosities of the mixtures, in themselves, give valuable information on compound formation in the system.

Viscosity of Mixtures.—The relation between kinematic viscosity and nitrosamine concentration is shown in Fig. 1 for several temperatures in the range +16° to −33°. The viscosity isotherms were constructed from the results of temperature–viscosity curves obtained for a series of mixtures in the range 39—100 mol. % of diethylnitrosamine. The isotherms for the lower temperatures terminate sharply at the composition at which the mixture solidified. The kinematic viscosity ν for liquid dinitrogen tetroxide was calculated from the data of Thorpe and Rodger (*Phil. Trans.*, 1894, **185**, *A*, 397) and of Pascal and Garnier (*Bull. Soc. chim.*, 1919, **15**, 309). Values of ν (in centistokes) for pure diethylnitrosamine are given in the following table:

Temperature	−33·0°	−26·9°	−20·7°	−14·4°	−7·9°	−1·5°	4·5°	11·5°	19·0°
Kinematic viscosity	3·61	3·07	2·65	2·31	2·02	1·82	1·62	1·47	1·28

At −33° the viscosity passes through a pronounced maximum (Fig. 1) with changing concentration, and the peak of the curve occurs at a composition equivalent to the compound, $N_2O_4{,}2Et_2N{\cdot}NO$. With increasing temperature the maximum becomes less pronounced, until at 16° it is scarcely perceptible. However, throughout the full temperature range the position of the maximum on the concentration axis remains constant. These results are readily explained on the assumption that only one compound, *viz.*, $N_2O_4{,}2Et_2N{\cdot}NO$, is present in the mixture, and that this compound is thermally unstable, so that the equilibrium

$$N_2O_4 + 2Et_2N{\cdot}NO \rightleftharpoons N_2O_4{,}2Et_2N{\cdot}NO \quad (B)$$

is displaced towards the left-hand side with increasing temperature.

* Part X, *J.*, 1951, 2843.

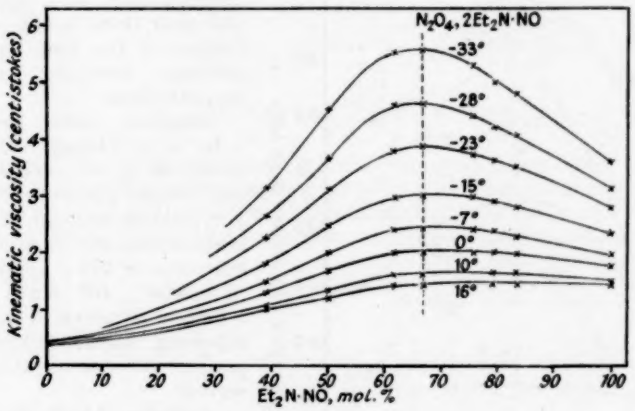
Electrical Conductivity of Mixtures.—Specific conductivities have been measured over a temperature range for mixtures of four different compositions and are recorded in columns (*a*) of Table 1. In each case, there is a linear relationship between κ and the temperature.

TABLE 1.*

$Et_2N{\cdot}NO$, mol. % ...	40·0		50·6		61·6		72·2	
Temp.	(*a*)	(*b*)	(*a*)	(*b*)	(*a*)	(*b*)	(*a*)	(*b*)
10°	2·620	2·83	2·490	3·39	2·660	4·25	2·165	3·48
0	2·350	3·08	2·155	3·64	2·285	4·56	1·840	3·68
− 7	2·165	3·32	1·925	3·87	2·025	4·85	1·610	3·88
−15	1·945	3·64	1·655	4·12	1·715	5·10	1·355	4·08
−23	1·735	4·04	1·390	4·36	1·410	5·34	1·120	4·27
−28	1·600	4·34	1·225	4·55	1·210	5·55	0·975	4·41
−33	1·465	4·79	1·055	4·83	1·020	5·61	0·830	4·52

* (*a*) = Specific conductivity $\kappa \times 10^{-4}$ ohm^{-1} cm.$^{-1}$; (*b*) = " corrected " conductivity $\kappa\eta/d \times 10^{-6}$.

FIG. 1.



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$Et_2N{\cdot}NO$, mol. %	40	50·6	61·6	72·2
Temp. coeff. $\times 10^{-4}$ (ohm^{-1} cm.$^{-1}$/degree)	0·0269	0·0334	0·0380	0·0312

It is of interest that the temperature coefficients pass through a maximum in the region of the composition N_2O_4,2$Et_2N{\cdot}NO$.

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Conductivity Isotherms.—The above conclusions were confirmed by the preparation of conductivity isotherms at three widely separated temperatures (shown as full curves in Fig. 2). As temperature decreases, the maximum becomes less pronounced. At 16° and 0° the maximum occurs at the 1 : 2 mol. ratio, but at −23° the curve is flattened to such an extent that it is not possible, from the specific conductivity measurements, to determine the position of the maximum. The same three isotherms, corrected for viscosity, are shown in

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−23	1·735	4·04	1·390	4·36	1·410	5·34	1·120	4·27
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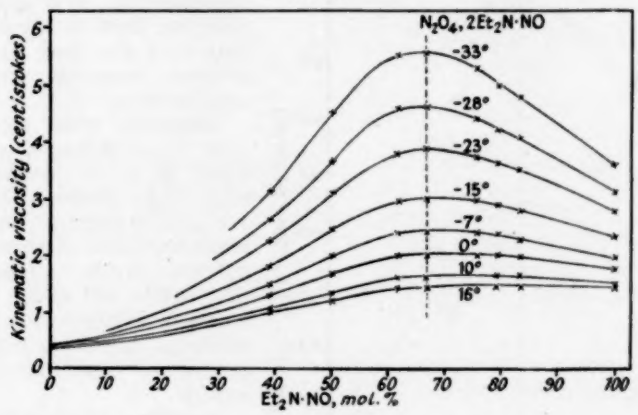
FIG. 1.



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$Et_2N{\cdot}NO$, mol. %	40	50·6	61·6	72·2
Temp. coeff. $\times 10^{-4}$ (ohm^{-1} cm.$^{-1}$/degree)	0·0269	0·0334	0·0380	0·0312

It is of interest that the temperature coefficients pass through a maximum in the region of the composition N_2O_4,2$Et_2N{\cdot}NO$.

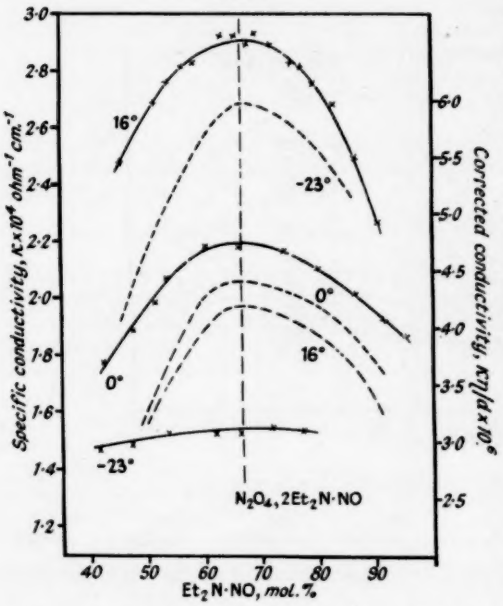
Allowance has been made for the variation in viscosity with temperature by the calculation of " corrected " conductivity values which are given in columns (*b*) of Table 1. Whereas the specific conductivity values have a positive temperature coefficient at all concentrations, the corrected conductivity shows a negative coefficient, and it is the corrected values which are to be related to changes in the position of the equilibrium with temperature. Neither liquid dinitrogen tetroxide nor diethylnitrosamine has an appreciable conductivity alone, and the relatively high electrical conductivity of the mixture arises from ionic dissociation of the compound N_2O_4,2$Et_2N{\cdot}NO$. The viscosity measurements above suggest that this compound is thermally unstable; increase in temperature will therefore reduce the proportion of compound (and the ionic concentration) in the system. This effect leads directly to a negative temperature coefficient for the corrected conductivity.

Conductivity Isotherms.—The above conclusions were confirmed by the preparation of conductivity isotherms at three widely separated temperatures (shown as full curves in Fig. 2). As temperature decreases, the maximum becomes less pronounced. At 16° and 0° the maximum occurs at the 1 : 2 mol. ratio, but at −23° the curve is flattened to such an extent that it is not possible, from the specific conductivity measurements, to determine the position of the maximum. The same three isotherms, corrected for viscosity, are shown in

Fig. 2 by broken curves. The maxima on the corrected conductivity curves are equally pronounced at all three temperatures, and each maximum occurs at the 1 : 2 mol. ratio. In agreement with measurements on solutions of fixed composition (Table 1), the specific conductivities show a positive temperature coefficient throughout the concentration range studied, whereas the corrected conductivities decrease with increasing temperature. On comparison of the shapes of the full and the broken curves, it becomes clear that the flattening of the peak in the specific conductivity curves, which occurs progressively as temperature is decreased, arises from the increasing viscosity of the mixtures.

Since, on a formal analogy with other solvent systems, diethylnitrosamine represents a "free base" in the liquid dinitrogen tetroxide solvent system (Part V, *J.*, 1951, 1298), it was important to identify as far as possible the ionic species present in these solutions. As a preliminary to this investigation, the direct current–voltage relationship has been determined for several concentrations. Ohm's law is obeyed throughout the voltage range employed, and at all concentrations, so it appears improbable that there is any change in the nature of the ionic species and/or electrode processes with changing concentration.

FIG. 2.



Solutions were electrolysed at −10° in an H-shaped cell containing about 30 g. of solution, and fitted with bright platinum electrodes. In a typical experiment, using 30% diethylnitrosamine solution, a potential difference of 220 v applied to the cell ($R = 4{\cdot}35 \times 10^4$ ohms) gave rise to a current of about 5 milliamp. The following effects (which are independent of concentration) were observed:

Cathode. After several minutes, the liquid in the immediate vicinity of the electrode became green; after one hour the liquid in the cathode limb developed the brown colour characteristic of dilute solutions of dinitrogen trioxide in the tetroxide. These effects indicate the liberation of nitric oxide, which is presumed to arise from the discharge of a nitrosonium (NO^+) ion.

Anode. No visible effects occurred at this electrode.

The following modes of ionisation are to be considered in the light of these electrode effects.

(*a*) The nitrosonium ion may result from the ionisation of the N_2O_4 molecule: $N_2O_4 \rightleftharpoons NO^+ + NO_3^-$. The nitrate ion so formed might be expected to discharge at the anode as follows:

$$NO_3^- \longrightarrow NO_2 + \tfrac{1}{2}O_2 + e \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\text{or} \quad NO_3^- \longrightarrow NO_2^+ + \tfrac{1}{2}O_2 + 2e \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The nitrosamine acts as a depolariser to prevent evolution of oxygen gas.

(*b*) The nitrosonium ion may result from the fission of the N–N bond in diethylnitrosamine, either directly

$$Et_2N \cdot NO \rightleftharpoons NO^+ + Et_2N^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

or, if we write the compound $N_2O_4,2Et_2N \cdot NO$ in the form of $NO_2,Et_2N \cdot NO$, by the ionisation

$$NO_2,Et_2N \cdot NO \rightleftharpoons N_2O_3^+ + Et_2N^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Goulden, Ingold, and Millen (*Nature*, 1950, **165**, 565) have shown by spectroscopic measurements that the nitrosonium ion may form a molecular complex $N_2O_3^+$ with nitrogen dioxide. Little is known of the diethylamine ion Et_2N^-, but it is reasonable to consider its existence since the unsubstituted amine ion NH_2^- is a common feature in reactions in liquid ammonia. Considering ionisation (4), discharge of $N_2O_3^+$ ions at the cathode would give rise to dinitrogen trioxide, as observed; electrolysis would result in the decomposition of one g.-mol. of diethylnitrosamine per Faraday.

Electrolytic Oxidation.—In view of the chemical reaction which takes place between diethylnitrosamine and liquid dinitrogen tetroxide on long standing (Part VI, *loc. cit.*), it is necessary to complete electrolytic experiments in a short time. In order to increase the proportional change in the concentration of the nitrosamine taking place during electrolysis, the small capacity cell shown in Fig. 3 was employed. The diethylnitrosamine was determined before and after electrolysis, and the results are collected in Table 2.

TABLE 2.

Composition of original solution, g.: $Et_2N{\cdot}NO$	N_2O_4	Faradays passed ($\times 10^{-4}$)	$Et_2N{\cdot}NO$ decomposed, (by analysis)	$Et_2N{\cdot}NO$ decomposed, g. (calc. from Eqn. 4)	$Et_2N{\cdot}NO$ oxidised, g. (calc. from Eqn. 5)
0·560	1·537	5·60	0·012	0·057	0·010
0·579	1·242	10·1	0·004	0·103	0·019
0·576	2·034	2·61	0·008	0·028	0·005
1·176	2·163	19·9	0·035	0·202	0·037

The quantities of diethylnitrosamine decomposed during electrolysis (col. 4, Table 2) are little more than the experimental error in analysis (see p. 1398), but are clearly of a different order of magnitude from the quantities (col. 5) required by equation (4). Nevertheless, analysis leaves no doubt that a very small quantity of nitrosamine is decomposed during

FIG. 3.

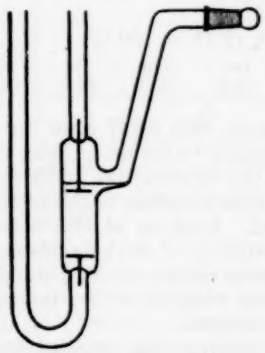
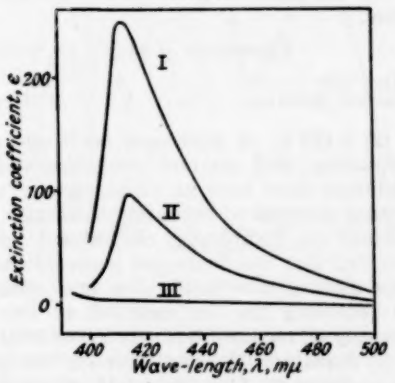


FIG. 4.



electrolysis. Ionisation schemes (3) and (4), being eliminated there are three agents which may be responsible for the oxidation of diethylnitrosamine: (*a*) nascent oxygen, produced by anode process (1); (*b*) the nitronium ion, produced in process (2); (*c*) in anode process (2), the NO_2^+ ions are produced in a medium containing NO_3^- ions. This combination of ions is equivalent to a solution of dinitrogen pentoxide in the liquid. Separate experiments have therefore been carried out to determine whether nitronium salts, and dinitrogen pentoxide, are able to oxidise diethylnitrosamine under normal conditions.

Reaction between Nitronium Pyrosulphate and Diethylnitrosamine.—About 0·5 ml. of diethylnitrosamine was added to about 0·2 g. (colourless crystals) of nitronium pyrosulphate. A violent reaction occurred immediately, with the evolution of oxides of nitrogen, acetaldehyde, and acetic acid. Under controlled conditions it is unlikely that the reaction would be arrested at the acetaldehyde stage; the reaction is clearly oxidative.

Reaction between Dinitrogen Pentoxide and Diethylnitrosamine.—The addition of pure diethylnitrosamine to solid dinitrogen pentoxide caused an almost explosive reaction, similar in character to the foregoing reaction. Much acetaldehyde was evolved. On addition of the nitrosamine to a 20% solution of dinitrogen pentoxide in the tetroxide, a less violent reaction occurred, so the reaction could be controlled by dilution of the reactants with dinitrogen tetroxide.

The experiments described below may be correlated on the assumption that diethylnitrosamine undergoes oxidation according to the equation

$$2(C_2H_5)_2N{\cdot}NO + 5\tfrac{1}{2}O_2 = 2C_2H_5{\cdot}NO_2 + 2CH_3{\cdot}CO_2H + HNO_2 + HNO_3 \quad . \quad (5)$$

followed by

$$C_2H_5{\cdot}NO_2 + HNO_2 = CH_3{\cdot}C(:NOH){\cdot}NO_2 + H_2O \quad . \quad . \quad . \quad . \quad (6)$$

Ethylnitrolic acid gives a coloured anion in alkaline solution; the solution is yellow when very dilute.

(*a*) When freshly prepared mixtures of diethylnitrosamine and liquid dinitrogen tetroxide were hydrolysed in aqueous potassium hydroxide solution, colourless solutions were obtained. When electrolysed mixtures were hydrolysed similarly, the resulting aqueous solutions were invariably pale golden-yellow.

(*b*) Nitroethane, equivalent in quantity to the diethylnitrosamine decomposed during electrolysis (Table 2), was added to a volume of potassium hydroxide solution (containing an excess of potassium nitrite) equal to that employed for hydrolysis of the electrolysed mixtures. On addition of acid (insufficient to neutralise the solution) a yellow colour developed, and the resulting solution could not be distinguished from the solution obtained by hydrolysis of the electrolysis products. Some ethylnitrolic acid may be produced in the nitrosamine–tetroxide mixture during electrolysis, but the major portion is considered to be formed during hydrolysis of the tetroxide.

(*c*) The oxidation products increase the electrical conductivity of the mixture, as shown below.

Electrolysis of 35·2% $Et_2N{\cdot}NO$ *solution in* N_2O_4 (P.D. = 220 v)

Time (min.)	0	25	53	81	100	130	170	200
Current (milliamp.)	9·9	11·1	11·9	13·6	15·0	18·0	26·0	36·0

(*d*) 0·125 G. of dinitrogen pentoxide was allowed to react with 0·747 g. of diethylnitrosamine, each reactant being dissolved in 3 ml. of dinitrogen tetroxide. Under these conditions there were no visible signs of reaction. When the mixture was added to an aqueous solution of potassium hydroxide, a yellow colour (characteristic of the solutions obtained on hydrolysing electrolysed mixtures) developed. Analysis of this solution indicated that the dinitrogen pentoxide had reacted with 0·023 g. of diethylnitrosamine. Since dinitrogen tetroxide does not oxidise diethylnitrosamine except on long standing, the pentoxide may be regarded, in this reaction, as being reduced to the tetroxide. Equation (5) requires the oxidation of 0·0215 g. of diethylnitrosamine.

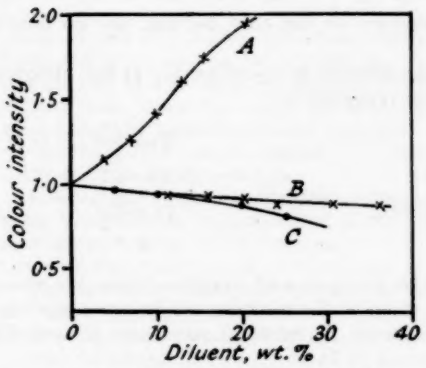
(*e*) Equation (5) being assumed, the quantities of diethylnitrosamine oxidised during the course of the four electrolytic experiments described in Table 2 have been calculated. The results (shown in col. 6, Table 2) are similar in order to the analytical values.

The Rôle of Diethylnitrosamine.—Light-absorption measurements (and experiments described in the following paper) provide evidence that diethylnitrosamine molecules are co-ordinated with the nitrosonium ions. Curve I (Fig. 4) is the extinction coefficient curve for a solution of nitrosonium hydrogen sulphate in diethylnitrosamine. The curve shows one sharp maximum at 412·5 mμ; there is appreciable absorption throughout the blue region of the visible spectrum. Such absorption is not a property of the nitrosonium or hydrogen sulphate ions alone, and since the curve was derived by employing dilute solutions of the nitrosonium compound, with diethylnitrosamine in the solvent compensating cell, the absorbing species must arise by association of the solvent with one or other of the solute ions. No colour develops when the hydrogen sulphate ion (in the form of the sodium salt or sulphuric acid) is added to diethylnitrosamine; we therefore conclude that the

observed absorption arises from association of the nitrosamine molecules with the nitrosonium ion. Curve II (Fig. 4) was obtained with dilute solutions of dinitrogen tetroxide in diethylnitrosamine, and is very similar in form to curve I. The peak occurs at 414 mμ; the slight shift from 412·5 mμ (curve I) may be attributed to the change in anion. Although the ionic nature of nitrosonium hydrogen sulphate probably leads to its complete ionisation in diethylnitrosamine solution, this will not be the case with dinitrogen tetroxide. Consequently, the concentration of absorbing species will be less than the stoicheiometric concentration of dinitrogen tetroxide from which the ε values (curve II) were calculated, and the ε values are therefore smaller than for curve I. Nevertheless, it is clear that the same absorbing species is present in each solution. Curve III was obtained for a solution of dinitrogen tetroxide in carbon tetrachloride; there is no longer a peak in the curve over this wave-length range, and the slight absorption may be attributed to the nitrogen dioxide present in equilibrium with the tetroxide (Lambrey and Corbière, *Compt. rend.*, 1935, **201**, 1334).

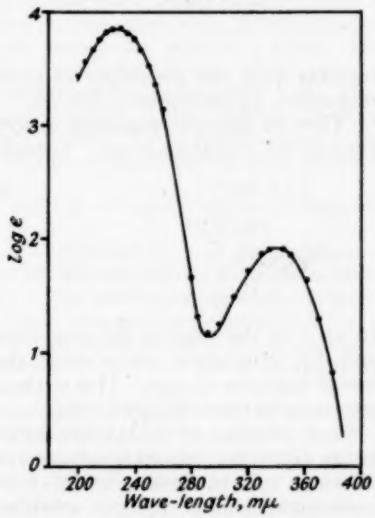
In order to determine the extinction coefficients for nitrosamine–tetroxide mixtures, it was necessary to use mixtures containing only about 1% of dinitrogen tetroxide. To

FIG. 5.



Liquid dinitrogen tetroxide diluted with:
$A = Et_2N{\cdot}NO$, $B = CCl_4$, $C = C_6H_5{\cdot}NO_2$.

FIG. 6.

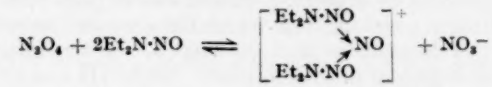


confirm the formation of a coloured compound in mixtures rich in tetroxide, the pure liquid tetroxide was diluted with diethylnitrosamine, and the variation in colour intensity compared (in a Duboscq colorimeter) with the corresponding variation when the tetroxide was diluted with carbon tetrachloride and with nitrobenzene. In each case the same artificial colour standard, an aqueous solution of methyl-orange and picric acid, was used. The results obtained at 18° are shown in Fig. 5. The vertical (colour intensity) units represent the depth of artificial standard solution required to match the experimental solution, pure dinitrogen tetroxide being regarded as unity. Although the diethylnitrosamine and nitrobenzene were pale yellow, the contribution of this colour is negligible compared with the intense colour due to the nitrogen dioxide present at 18°. On dilution with the inert solvents carbon tetrachloride and nitrobenzene, a gradual decrease in colour intensity was observed which is consistent with the decreasing concentration of nitrogen dioxide in the solutions. In spite of this, the colour intensity produced on dilution with diethylnitrosamine increases sharply.

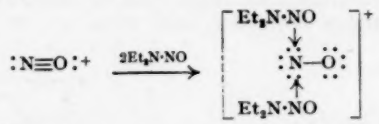
The conductivity of the tetroxide–nitrosamine mixtures, although large in comparison with the conductivity of the pure components (Part VI, *loc. cit.*), is too small to enable suitable transport measurements to be carried out. When the electrodes are placed at a

sufficient distance to avoid mixing of the contents of the electrode compartments, it is necessary to continue the electrolysis for a considerable time in order to obtain any detectable change in the distribution of nitrosamine in the cell. Before this stage can be reached, the irreversible reaction between the components takes place, and this vitiates the analyses.

Structure of Cation.—Since diethylnitrosamine and dinitrogen tetroxide react in the 2 : 1 ratio only, the equilibria in the system may be represented as :

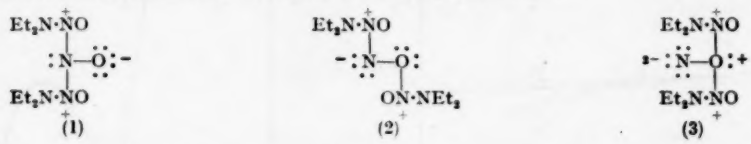


The NO^+ ion has a total of 10 valency electrons; the addition of two electron pairs involves the completion of the electron octet for both the nitrogen and the oxygen atom, with the two atoms then united by a single electron-pair bond. The electron rearrangements involved in the process



together with the possibility of extensive resonance in the complex ion, are no doubt responsible for the colour of the ion.

The two diethylnitrosamine molecules are represented as co-ordinating at the nitrogen atom of the nitrosonium ion. Consider the three possibilities :



In view of the relative electron affinities of the nitrogen and oxygen atoms, the most probable structure is one in which the oxygen atom of the nitrosonium group carries the formal negative charge. This is the case in structure (1), whereas structures (2) and (3) appear to be much less probable.

Since solutions of diethylnitrosamine in dinitrogen tetroxide are considered as " basic " in the dinitrogen tetroxide solvent system, it is of interest that the ion $[(Et_2N{\cdot}NO)_2NO]^+$, shown to exist in these solutions, is formally analagous to the ammonium, or substituted ammonium, ions in aqueous solutions of ammonia or amines, in that it represents the association of the free base with the cation characteristic of the solvent.

Experimental

Measurement of Viscosities.—In correcting conductivity results for the effects of viscosity, the dynamic viscosity η has been employed by Usanovich (*Compt. rend. Acad. Sci.*, U.S.S.R., 1939, **25**, 608) and others. However, there appears to be considerable justification for employing the expression $\kappa\eta/d$, where d is the density, as the " corrected conductivity " σ, since the result then refers to the conductivity of a unit mass (1 g.) of material placed between electrodes 1 cm. apart (Allmand and Nickels, *Nature*, 1923, **112**, 862). The term η/d (the kinematic viscosity ν) is available directly from the viscometer measurements without separate measurement of the density of the liquid. This procedure has been used in the present work.

The instrument used was an Ostwald-type U-tube viscometer, constructed in Pyrex glass; the open ends of the vertical limbs were fitted with B14 ground-glass sockets carrying drying tubes of potassium hydroxide pellets, which protected the contents from atmospheric moisture but allowed an unrestricted passage of air to and from the apparatus. The volume of the upper bulb was 6·5 ml.; the capillary tube was 10 cm. long (bore diameter 0·7 mm.).

Constant volumes of the liquid mixtures were made up by weighing into a 10-ml. graduated flask fitted with a side-arm, through which the contents could then be poured in a closed system

into the viscometer *via* the ground joint on the reservoir limb. The liquid was brought into the upper bulb before each timed run by applying pressure to the reservoir limb rather than by using suction on the capillary limb, to avoid the formation of vapour locks in the capillary. Times of flow varied from 80 to 380 seconds.

The kinematic viscosity was determined by using the expression $\nu = At - Bt^{-1}$; B was calculated from the dimensions of the apparatus and had a value of 2·90 centistokes sec.; A was determined by measuring the time of flow of distilled water and of pure nitrobenzene and had a value of 1·454 centistokes sec.$^{-1}$

Measurements were made on dinitrogen tetroxide–diethylnitrosamine mixtures over the temperature range −33·0° to +11·5°. The viscometer was placed in a bath of alcohol cooled by solid carbon dioxide. By means of an efficient mechanical stirrer, and judicious addition of solid carbon dioxide, the temperature could be controlled to ±0·15° at the lower end of the range, and to ±0·05° at the higher temperatures. Because of this, and since the temperature coefficient of viscosity increases with diminishing temperature, the results obtained were of a somewhat lower order of accuracy at the lower than at the higher temperatures. The design of the instrument was such that the change in the hydrostatic head of the liquid arising from changes in volume was rather less than 1% over the temperature range employed. These various effects lead to an overall experimental error between 1% and 2%, depending on temperature.

Temperature Coefficient of Electrical Conductivity.—The cell used (liquid capacity about 3 ml.) is shown in Fig. 3. It was constructed in Pyrex glass and was fitted with lightly platinised platinum electrodes placed about 2·5 cm. apart. The cell constant had a value of 0·460. The mixtures were made up by distilling a known weight of diethylnitrosamine under reduced pressure into a 10 × 1·5 cm. tube fitted with a side-arm carrying a B10 ground-glass cone. Pure dinitrogen tetroxide was then distilled in to the required composition, and the mixture filled into the cell by attaching the latter to the B10 joint and suitably tilting the apparatus: the cell was then closed by a tight-fitting stopper. The resistance measurements were made by using a Mullard Measuring Bridge Type G.M. 4140/1.

The temperature range covered was −33·0° to +10° and the control was similar to that used in the viscosity measurements.

Conductivity Isotherms.—In determining the variation of conductivity with the composition of the mixtures, the apparatus and the technique employed were essentially the same as those used in determining the 0° isotherm in Part VI (*loc. cit.*). The curves relating conductivity (or viscosity) with temperature were of such a form as to permit accurate extrapolation to 16°.

Current–Voltage Curves.—The current–voltage curves for mixtures of diethylnitrosamine and liquid dinitrogen tetroxide were measured in a cell similar to that used for the conductivity of the pure liquid tetroxide (Part III, *J.*, 1951, 1289, Fig. 3).

Diethylnitrosamine was purified as described in Procedure C, Part VI (*loc. cit.*), and the mixtures were made up by weighing the cell after the addition of each of the components. The measuring circuit consisted of a simple voltmeter–microammeter arrangement; the microammeter was a Pye " Scalamp " multi-range instrument and was calibrated before use. The following results show the direct proportionality between current and voltage, v being given in volts and c in microamp.

Electrolysis Experiments.—In the electrolytic measurements from which the results in Table 2 were obtained, the cell (Fig. 3) was immersed in a bath of alcohol and solid carbon dioxide at −10° to prevent the boiling of the dinitrogen tetroxide–diethylnitrosamine mixtures which

23·4 Mol. % $Et_2N{\cdot}NO$ (R at 1000 c/s = 2·0 × 10^3 ohms)

v	0·044	0·200	0·300	0·400	0·500	0·600	0·700	0·800	0·900	1·050
c	22·4	100·5	149	196	244	290	339	386	434	506
$v/10^3c$	1·97	1·99	2·01	2·04	2·05	2·06	2·06	2·07	2·07	2·07

28·8 Mol. % $Et_2N{\cdot}NO$ (R at 1000 c/s = 0·945 × 10^3 ohms)

v	0·100	0·202	0·300	0·400	0·500	0·600	0·700
c	107	211	318	422	528	630	750
$v/10^3c$ ...	0·934	0·948	0·944	0·948	0·949	0·952	0·934

69·0 Mol. % $Et_2N{\cdot}NO$ (R at 1000 c/s = 4·85 × 10^3 ohms)

v	0·100	0·400	0·500	0·600	0·700	0·800	0·900	1·000	1·100
c	20·0	84·0	106	126	145	164	182	201	224
$v/10^3c$ ...	5·00	4·77	4·72	4·76	4·82	4·88	4·93	4·96	4·90

79·3 Mol. % $Et_2N{\cdot}NO$ (R at 1000 c/s = 6·30 × 10^3 ohms)

v	0·100	0·200	0·300	0·600	0·700	0·800	0·900	1·000	1·100
c	16·0	31·2	46·9	98·0	112	126	140	156	170
$v/10^3c$ ...	6·24	6·40	6·49	6·13	6·25	6·34	6·42	6·40	6·48

otherwise occurred as a result of the heating effects of the current; 220 volts d.c. was applied, the current being measured on a milliammeter in series with the cell. Since the current passing increased with time, it was noted at 10-minute intervals during the electrolysis, and the quantity of electricity was found from the area under the curve obtained by plotting current against time. A check experiment using an iodine coulometer showed that this procedure gave results of sufficient accuracy.

After electrolysis, the contents of the cell were hydrolysed in an aqueous solution of potassium hydroxide, and the diethylnitrosamine determined as described below.

Determination of Diethylnitrosamine.—This was carried out by measurements of the ultraviolet absorption spectrum of the hydrolysed solutions, a " Unicam " S.P. 500 spectrophotometer being used with 1-cm. quartz cells and a hydrogen-discharge lamp as the source of radiation. The absorption spectrum obtained for solutions of pure diethylnitrosamine in distilled water is shown as the full curve in Fig. 6. (This curve is distinct from the experimental points shown in Fig. 6, which are discussed below.) The curve shows two maxima, at 227·5 mμ ($\varepsilon = 7400$) and 340·0 mμ ($\varepsilon = 85$). The maximum at 340 mμ is well suited for quantitative analyses, since the optical density D for solutions about 0·005M in nitrosamine is in the range 0·25—1·0 when measured in 1-cm. cells, and at this order of concentration Beer's law is accurately obeyed at 340 mμ. This is shown by the following results:

$Et_2N{\cdot}NO$ concn. (M)	0·00242	0·00472	0·00514	0·00943
D at 340 mμ	0·262	0·402	0·440	0·800
ε	85·5	85·2	85·7	84·8

The solutions to be analysed also contained nitrite and nitrate formed by hydrolysis of dinitrogen tetroxide, and both these ions absorb significantly at 340 mμ. This difficulty was overcome by taking advantage of the high volatility in steam of diethylnitrosamine. A typical experiment is described below.

10 Ml. of an aqueous solution of diethylnitrosamine (0·0199 g.-mol./l.) were treated with 5 g. of potassium hydroxide and 0·1 g. each of potassium nitrite and nitrate, and diluted with water to 50 ml. in a 100-ml. flask. A small water condenser was attached to the flask, and the solution was distilled gently for 15—20 minutes. All the nitrosamine distilled in the first 25 ml. of aqueous distillate. The optical density of the distillate was measured at 340 mμ. Triplicate analyses gave concentrations of 0·0200, 0·0201, and 0·0199 g.-mol. of nitrosamine per litre in the original solution.

The above procedure was applied to the determination of diethylnitrosamine in admixture with liquid dinitrogen tetroxide. Known weights (about 0·5 g.) of the two liquids were mixed in a small, stoppered, sample tube. The mixture was hydrolysed by adding it to 250 ml. of N-potassium hydroxide solution in a stoppered vessel. The solution was diluted to 500 ml., and 25-ml. aliquots were treated as described above. The quantity of nitrosamine taken was 0·580 g.; analysis gave 0·571 g.

If electrolysis of tetroxide–nitrosamine mixtures produced any compound which was volatile in steam when distilled from alkaline solution, and which absorbed at 340 mμ, the above method of analysis would be vitiated. An electrolysed mixture was therefore hydrolysed, and the values of D between 200 and 400 mμ were determined on the aqueous distillate. The absorption at 340 mμ being assumed to be due only to diethylnitrosamine, ε values over the 200—400 mμ range were calculated. These values are shown as experimental points in Fig. 6, and are seen to correspond exactly with the absorption curve for pure diethylnitrosamine.

Controlled Reaction between Dinitrogen Pentoxide and Diethylnitrosamine.—Dinitrogen pentoxide was prepared by Daniels and Bright's method (*J. Amer. Chem. Soc.*, 1920, **42**, 1131). A known weight of it (about 0·12 g.) was condensed in a 5 × 1 cm. tube having a B14 ground-glass cone at its open end. The pentoxide was not freed from an accompanying trace of dinitrogen tetroxide but was dissolved directly in 3 ml. of the pure tetroxide. About 0·7 g. of pure diethylnitrosamine was dissolved in 3 ml. of dinitrogen tetroxide in a similar tube fitted with a B14 socket. With both tubes closed by guard-tubes of phosphoric oxide, the contents of each were frozen completely solid; the guard-tubes were removed and the dinitrogen pentoxide tube was inverted and fitted to the top of the nitrosamine tube. The latter being kept frozen, the solution of the pentoxide was allowed to melt slowly and run down into the solid nitrosamine solution, where it resolidified. When the transfer was complete, the mixture was melted and kept at room temperature for 15 minutes. It was then added to aqueous alkali, and the nitrosamine determined.

Preparation of Nitronium Pyrosulphate.—Nitronium pyrosulphate, $(NO_2)_2S_2O_7$, was prepared

as described by Goddard, Hughes, and Ingold (*J.*, 1950, 2559), from pure dinitrogen pentoxide and sulphur trioxide (1 : 2) in nitromethane solution. After it had dried in a vacuum over phosphoric oxide, its purity was tested by determining the acid equivalent weight (Found: 45·0. Calc.: 44·7). This agreement was taken as evidence that little if any free acid was present in the product.

Extinction Curve for the Ion $(Et_2N{\cdot}NO)_2NO^+$.—The ε values recorded in Fig. 4 were obtained by using the " Unicam " spectrophotometer. In order to avoid the preparation of solutions containing less than about 1% of the nitrosonium compound, it was found convenient to use 2-mm. (rather than 1-cm.) optical cells. Nitrosonium hydrogen sulphate was prepared by the method of Angus and Leckie (*Proc. Roy. Soc.*, 1935, **149**, *A*, 327).

Colorimetric Measurements.—The artificial standard solution was contained in the normal Duboscq plunger-type cup. The cell containing the dinitrogen tetroxide mixtures was prepared by sealing a 2-mm. cell at right angles to the bottom of a 4 × 1 cm. tube, to form the lower limb of an L-shaped unit. The liquid was viewed through the optical faces of the cell, which were held horizontal. The colorimeter was modified to permit the immersion of the cell in a bath kept at 18°, and having an optically plane base.

THE UNIVERSITY, NOTTINGHAM. [*Received, October 27th*, 1951.]

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255. *The Liquid Dinitrogen Tetroxide Solvent System. Part XII.* Amphoteric Reactions involving Zinc Compounds.*

By C. C. ADDISON and C. P. CONDUIT.

Metallic zinc reacts readily with solutions of diethylnitrosamine in liquid dinitrogen tetroxide with evolution of nitric oxide and the formation of a red liquid immiscible with dinitrogen tetroxide. This liquid product is indistinguishable from that formed by dissolving the compound $Zn(NO_3)_2.2N_2O_4$ in diethylnitrosamine, or by adding dinitrogen tetroxide to a solution of anhydrous zinc nitrate in diethylnitrosamine. Colorimetric and spectroscopic measurements show that the state of the liquid product may be represented by the equilibrium

$$Zn(NO_3)_2 + 2N_2O_4 + 4Et_2N{\cdot}NO \rightleftharpoons [(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4]$$

The reaction of metallic zinc is represented as:

$$Zn + 4N_2O_4 + 4Et_2N{\cdot}NO \rightleftharpoons [(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4] + 2NO$$

These reactions are analogous to the corresponding reactions of zinc hydroxide, and of metallic zinc, with aqueous solutions of alkali hydroxides.

METALLIC zinc has been found to react rapidly with solutions of " bases " in liquid dinitrogen tetroxide. Since diethylnitrosamine is able to enhance the ionisation of the tetroxide, its presence in the system increases the concentration of NO_3^- ions (Part XI, preceding paper), and in consequence metallic zinc reacts rapidly with these solutions. The present paper describes the reaction between metallic zinc or zinc nitrate and solutions of diethylnitrosamine in liquid dinitrogen tetroxide.

It was observed (by R. Thompson in this laboratory) that when a block of pure metallic zinc (about 5 g.) was added to about 15 ml. of a 30% solution of the nitrosamine at 15°, reaction commenced immediately, with rapid evolution of nitric oxide gas. The latter was recognised by closing the reaction vessel with a guard-tube containing activated alumina; this reagent absorbs nitrogen dioxide but not nitric oxide, which could be observed on oxidation in the atmosphere. Some nitric oxide dissolved in the liquid mixture, the colour of which changed within a few minutes to dark green, and at the end of one hour the liquid was opaque to strong light. The zinc compound(s) formed during reaction were readily soluble in the liquid mixture, so the surface of the zinc block remained bright throughout the reaction. On cooling, the liquid became highly viscous, and it was not possible to separate the reaction product in solid form by crystallisation.

* Part XI, preceding paper.

The addition of liquid dinitrogen tetroxide to the reaction mixture produced two liquid layers, and the reaction product appeared to be immiscible with the pure tetroxide. The above experiment was therefore repeated with a solution containing only 8% of diethylnitrosamine. As before, nitric oxide was rapidly evolved, but within one minute, globules of an immiscible liquid product were formed on the zinc surface. After one hour, this product collected as a lower liquid phase forming about 30% of the total liquid volume. This layer was found to have a high zinc and nitrosamine content; when dissolved nitric oxide was removed by warming, a red oil remained. The upper layer consisted of dinitrogen tetroxide, containing traces only of zinc compounds and diethylnitrosamine.

Rate of Reaction.—The increase in rate of reaction of zinc on addition of diethylnitrosamine to the liquid tetroxide is illustrated in the following table. The reaction rates in pure dinitrogen tetroxide are calculated from Part VIII (*J.*, 1951, 2833); the difference in the temperature at which the two experiments were carried out is approximately compensated by the different stirring conditions, so that the rates recorded in the table reflect the relative velocities of the two reactions.

	Wt. of Zn reacting (g. × 10^{-3}/cm.²)	
Period of immersion (min.)	(*a*) In liquid N_2O_4 alone (18·5°, stirring rate 250 r.p.m.)	(*b*) In 6·5% $Et_3N{\cdot}NO$ solution (15°, stirred by shaking)
5	0·24	4·7
10	0·47	9·3
15	0·69	14·0
30	0·84	27·0
45	0·90	39·3
60	0·96	51·6
90	—	75·0
120	—	95·4

Whereas the rate of reaction with pure tetroxide decreases after an immersion period of 15 minutes, this rate is almost independent of period of immersion in diethylnitrosamine solutions. The addition of 6·5% of diethylnitrosamine therefore increases the initial rate of reaction by a factor of 20, and this factor is increased considerably by longer periods of immersion.

The reaction with nitrosamine solutions, like the reaction with tetroxide alone, is strongly temperature dependent. This is illustrated below for 5·6% of diethylnitrosamine in liquid dinitrogen tetroxide:

Temp.	−12·2°	−7·0°	−0·5°	5·0°	10·0°
Wt. of Zn reacting (10^{-3} g./cm.²/15 min.)	1·57	2·23	5·01	7·23	9·11

Product of Reaction.—The product of reaction is obtained in the form of a red oil which is immiscible with liquid dinitrogen tetroxide. The following preliminary experiments were carried out to determine the nature of this oil.

(a) *Action of organic solvents.* The red oil was immiscible with chloroform, carbon tetrachloride, and chlorobenzene, but shaking with these solvents reduced the intensity of the red colour. The oil was immiscible with diethyl ether, but reacted rapidly at the liquid interface; acetaldehyde was recognised as a decomposition product. This reaction is significant in the light of the observation (Part VII, *J.*, 1951, 2829) that the compound $Zn(NO_3)_2{,}2N_2O_4$ also oxidises ether to acetaldehyde.

(b) *Thermal decomposition.* On warming to 40—50°, the colour of the oil deepened somewhat; at higher temperatures (up to about 80°) dinitrogen tetroxide evaporated rapidly, accompanied by a fading of the colour to pale yellow. No further change occurred thereafter until the temperature reached 170—180°, whereat diethylnitrosamine began to evaporate. At this stage the rate of thermal decomposition increased sharply, and unless the heating was carefully controlled, decomposition occurred explosively. The white solid which remained was identified as a mixture of zinc nitrate and zinc oxide.

These results suggest that the product of reaction consists of zinc nitrate combined with diethylnitrosamine and dinitrogen tetroxide. This has been confirmed by the preparation, directly from these three materials, of a red oil having the same properties as that prepared from metallic zinc. Anhydrous zinc nitrate is readily soluble in diethylnitrosamine to give

a colourless solution. The addition of dinitrogen tetroxide to this solution produced a deep red colour. The compound $Zn(NO_3)_2,2N_2O_4$ was also treated directly with diethylnitrosamine. The solid dissolved to give a deep red solution, and the red oils prepared by either of these two methods could not be distinguished from that prepared from metallic zinc. The reactions may be summarised as follows.

$$Zn + N_2O_4 \longrightarrow Zn(NO_3)_2,2N_2O_4 \xrightarrow{\text{heat}} Zn(NO_3)_2 + 2N_2O_4$$

$$\downarrow Et_2N{\cdot}NO \qquad\qquad \downarrow Et_2N{\cdot}NO$$

$$Zn + N_2O_4 + Et_2N{\cdot}NO \longrightarrow \text{Red oil} \xrightarrow{N_2O_4} \text{Colourless solution}$$

Phase Equilibria.—The results in Fig. 1 were obtained at 18°. In mixtures containing up to about 10% of diethylnitrosamine, the dinitrogen tetroxide phase contains very little of the zinc compound. Thereafter, the miscibility curve rises sharply in the direction of increasing zinc content. In the concentration range 5—10% of diethylnitrosamine, sufficient

FIG. 1.

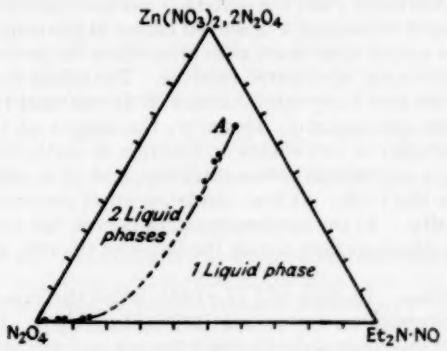


FIG. 2.

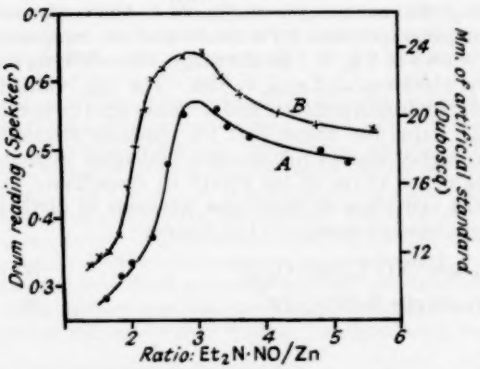
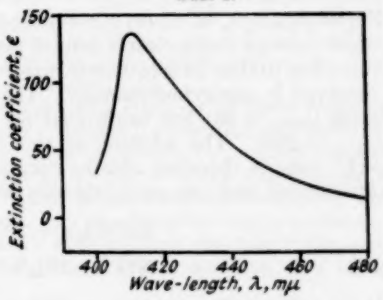


FIG. 3.



zinc is dissolved in about 1 minute to carry the system into the two-phase region. With 30% diethylnitrosamine solution the system is still homogeneous after 1 hour's reaction. The miscibility curve terminates at the invariant point *A*, which represents the composition of the system at which both liquid phases are saturated with the component $Zn(NO_3)_2,2N_2O_4$.

Constitution of Red Oil.—Attempts were made to determine the ratio of the constituents by measurement of the rate of solution of the compound $Zn(NO_3)_2,2N_2O_4$ in diethylnitros-

amine under various experimental conditions, it being expected that a break in the rate curve would occur when a quantity of the zinc compound had dissolved, equivalent to the nitrosamine present. No such break was observed. Attempts to obtain the constituent ratios by solvent extraction were also unsuccessful. Each of these experiments failed owing to the operation of an equilibrium between the compound and its constituents (see below).

(a) *Colorimetric analysis.* A known weight (about 1·5 g.) of $Zn(NO_3)_2,2N_2O_4$ was treated with successive small amounts of diethylnitrosamine in an optical cell. After each addition, the colour of the liquid was compared with that of an artificial standard in a Duboscq visual colorimeter. The results are shown as curve *A*, Fig. 2. The experiment was repeated in a " Spekker " photoelectric absorptiometer, and the results are shown as curve *B*. The shapes of the curves are closely similar; the addition of diethylnitrosamine produces at first a rapid increase in colour intensity, and the curves pass through a somewhat rounded maximum at a $Et_2N{\cdot}NO : Zn$ ratio of about 3 : 1. Thereafter a gradual fall in colour intensity occurs.

The shape of these curves supports the existence of an equilibrium $Et_2N{\cdot}NO + Zn(NO_3)_2,2N_2O_4 \rightleftharpoons$ coloured product, rather than an irreversible reaction proceeding from left to right. In the latter case, the system could be considered as consisting initially of a pure liquid compound containing a dissolved excess of the compound $Zn(NO_3)_2,2N_2O_4$. Additional nitrosamine would then react with this excess to produce a greater quantity, but not a greater concentration, of coloured product. The colour intensity should therefore remain constant until no zinc compound remains in excess, and then decrease gradually on dilution with further nitrosamine. However, the shapes of the curves (Fig. 2) are consistent with the operation of two effects on addition of diethylnitrosamine, (*a*) dilution of the mixture, causing a decrease in colour intensity, and (*b*) a displacement of the above equilibrium to the right-hand side. At first, the latter effect predominates, leading to a net increase in colour intensity. At the maximum on the curves, the equilibrium shift becomes almost complete, so the dilution effect is then the larger of the two, and the colour intensity falls.

(b) *Absorption spectrum.* In Part VII (*J.*, 1951, 2829) the compound $Zn(NO_3)_2,2N_2O_4$ was considered as a nitrosonium compound $(NO^+)_2[Zn(NO_3)_4]$. In Part XI (preceding paper) it was shown that mixtures of dinitrogen tetroxide and diethylnitrosamine contained the red ion $(Et_2N{\cdot}NO)_2NO^+$. On correlation of these facts, the red colour of the oil produced in the reaction of zinc with N_2O_4–$Et_2N{\cdot}NO$ mixtures is attributed to the compound $[(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4]^{2-}$. The absorption spectrum for a solution of the compound $Zn(NO_3)_2,2N_2O_4$ in diethylnitrosamine is shown in Fig. 3. In the range 400—500 mμ the curve shows a single clearly defined peak at 410·5 mμ, and $\varepsilon_{max.} = 136$. The $\lambda_{max.}$ value is very close to that for solutions of nitrosonium hydrogen sulphate and for dinitrogen tetroxide dissolved in diethylnitrosamine. The $\varepsilon_{max.}$ value lies above that for the pure tetroxide alone ($\varepsilon_{max.} = 95$) but below that for the highly ionised nitrosonium hydrogen sulphate ($\varepsilon_{max.} = 250$). The addition of zinc nitrate, by virtue of its ability to co-ordinate the NO_3^- ions, is therefore able to enhance the ionisation of dinitrogen tetroxide in diethylnitrosamine, and two equilibria may be considered to operate in this system :

$$Zn(NO_3)_2 + 2N_2O_4 \rightleftharpoons (NO^+)_2[Zn(NO_3)_4]^{2-} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and

$$NO^+ + 2Et_2N{\cdot}NO \rightleftharpoons (Et_2N{\cdot}NO)_2NO^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

If the full equation for this reaction, *i.e.*,

$$Zn(NO_3)_2 + 2N_2O_4 + 4Et_2N{\cdot}NO = [(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4]^{2-}$$

proceeded irreversibly in the forward direction, this would require a break in the colour intensity curves (Fig. 2) at a $Et_2N{\cdot}NO : Zn$ ratio of 4 : 1. Equilibrium (1) above is responsible for the lower ratio observed experimentally. For example, in any system $A + 2B \rightleftharpoons C$, it may be shown that the equilibrium concentration of C is a maximum when the initial amounts of A and B taken are in the ratio 1 : 2. Both the above equilibria (1) and (2) are of this form. In (1), if the solution in diethylnitrosamine is prepared by using

the compound $Zn(NO_3)_2,2N_2O_4$, then the available concentration of nitrosonium ions is automatically at its maximum value. In (2), the ion $(Et_2N{\cdot}NO)_2NO^+$ being assumed to be responsible for colour, then the maximum colour intensity will occur when the initial concentrations of NO^+ and $Et_2N{\cdot}NO$ are in the ratio 1 : 2. If reaction (1) proceeded to completion, then the $Et_2N{\cdot}NO$: Zn ratio would be 4 : 1 at the colour maximum. However, the $\varepsilon_{max.}$ value determined from the absorption spectrum (Fig. 3) shows that reaction (1) is not complete, and in consequence the $Et_2N{\cdot}NO$: Zn ratio must fall below 4 : 1 to an amount dependent upon the equilibrium constant of equation (1). The observed ratio of 3 : 1 is therefore consistent with equilibria (1) and (2).

Amphoteric Nature of Reactions.—The reaction

$$Zn(NO_3)_2 + 2[(Et_2N{\cdot}NO)_2NO^+{\cdot}NO_3^-] \xrightarrow{\text{in } N_2O_4} [(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4]^{2-}$$

illustrates clearly the amphoteric properties of zinc nitrate in the liquid dinitrogen tetroxide solvent system. The analogous reaction in the aqueous system

$$Zn(OH)_2 + 2(Et_2NH{\cdot}H^+{\cdot}OH^-) \xrightarrow{\text{in } H_2O} (Et_2NH{\cdot}H^+)_2[Zn(OH)_4]^{2-}$$

does not take place because the available hydroxyl-ion concentration is not sufficiently great to stabilise the $[Zn(OH)_4]^{2-}$ ion, but the corresponding reaction involving alkali hydroxides $Zn(OH)_2 + 2NaOH = Na_2[Zn(OH)_4]$ is well known.

The close analogy between the reactions of metallic zinc described above and the reactions of zinc in the aqueous system is well illustrated by the following equations :

$$Zn + 2[(Et_2N{\cdot}NO)_2NO^+\ NO_3^-] + 2N_2O_4 = [(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4] + 2NO$$

and

$$Zn + 2NaOH + 2H_2O = Na_2[Zn(OH)_4] + H_2$$

Experimental

Three-component diagram. The data in Fig. 1 were obtained by adding dinitrogen tetroxide and diethylnitrosamine in approximately the desired quantities to 1—2 g. of solid $Zn(NO_3)_2,2N_2O_4$, contained in a 7 × 1·5 cm. stoppered tube. The mixture was kept with frequent shaking, in a water-bath at 18° for about one hour. From each layer, two weighed samples of liquid (about 0·5—1 g. depending upon the zinc and the diethylnitrosamine content) were withdrawn. One sample was ignited to zinc oxide, the weight of which was used to calculate the percentage of $Zn(NO_3)_2,2N_2O_4$. Diethylnitrosamine was determined in the second sample as follows. The sample was hydrolysed in water; a suitable aliquot was made 7N with respect to hydrochloric acid and the mixture was boiled for 2 hours under an efficient reflux. This was sufficient to complete the reaction $Et_2N{\cdot}NO + H_2O + HCl = Et_2NH_2Cl + HNO_2$. The reaction mixture was cooled and made strongly alkaline by careful addition of solid potassium hydroxide. The liberated diethylamine was then distilled into an excess of standard acid.

Colorimetric analysis. Methyl-red, sodium nitroprusside, and mixtures of these reagents were found to provide suitable colour standards. For the " Spekker " absorptiometer measurements a 10 × 2 mm. microcell (light path 2 mm.) was sealed longitudinally by means of Silicone cement to a 5 × 1 cm. glass tube. The tube was closed by a Silicone rubber plug carrying a microburette. The compound $Zn(NO_3)_2,2N_2O_4$ was placed in the cell, dissolved in the minimum quantity of diethylnitrosamine, and the titration carried out by adding successive additional quantities of diethylnitrosamine from the burette. After each addition, the colour intensity of the mixture was compared with that of the artificial colour standard contained in a 1-cm. optical cell, the " direct reading " method being used.

The University, Nottingham. [*Received, October 27th,* 1951.]

256. *Hypsochromic Shifts in Methylated Hydrocarbons.*

By H. C. Longuet-Higgins and R. G. Sowden.

Hypsochromic shifts produced by methyl substitution in certain unsaturated hydrocarbons are interpreted in terms of simple molecular orbital (M.O.) theory. It is shown that such shifts can only occur if one or more odd-membered rings are present, in general agreement with observation. The magnitudes of these effects calculated by second-order perturbation theory are in good agreement with those obtained by the longer procedure of solving the secular equations.

The introduction of an alkyl group into a non-alternant hydrocarbon (Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39) brings about, in some cases, a shift in the longest wave-length of absorption towards the violet. It seems worth while to attempt an interpretation of this effect in terms of simple molecular orbital (M.O.) theory because, in spite of objections, this theory has had successful applications in the field of molecular spectra. We shall consider separately the inductive and hyperconjugative effects of a methyl group, and shall apply our results specifically to the molecules azulene and fulvene.

In the ground state of a molecule, the electrons occupy the bonding orbitals in pairs, and it is usual to assume that excited states are obtained by promoting electrons from the bonding orbitals into the antibonding orbitals. The first excited state is obtained when an electron is transferred from the highest bonding orbital to the lowest antibonding orbital ($N \longrightarrow V_1$ transition, in Mulliken and Rieke's notation), and it is assumed that the longest wave-length of absorption is determined by the change in energy involved in this process. Hence a change in the nature of the molecule causing a decrease in the separation of these levels will be marked by a bathochromic shift, and a change causing an increase by a hypsochromic shift.

The introduction of an alkyl group into a hydrocarbon does in fact bring about a shift in the wave-length of maximum absorption, as is well known; and, in general, (1) the shift in the case of alternant hydrocarbons is invariably a bathochromic one, but (2) with non-alternant hydrocarbons, it may be either bathochromic or hypsochromic.

The first generalisation has been accounted for in a theorem by Dewar (*J.*, 1950, 2329), who, however, ignores the inductive effect of the entering group. As regards non-alternant hydrocarbons, Pullman has shown that hypsochromic shifts are to be expected in certain cases on the basis of simple M.O. theory, and need not necessarily be attributed to steric interference. Pullman, Mayot, and Berthier (*J. Chem. Phys.*, 1950, **18**, 257) solved the secular equations for all the methylated azulenes, and compared the energies of the $N \longrightarrow V_1$ transitions in these molecules with the transition energy for azulene itself. Their method is, however, rather laborious, and is of no general illustrative value. Instead, a method is available whereby the inductive and hyperconjugation effects of the entering alkyl group may be considered separately, and the separate effects added : not only does this method lead to qualitative agreement with observation, but it also illustrates the origin of the observed hypsochromic shifts.

The Inductive Effect.—When a boundary hydrogen atom is replaced by a methyl group, the Coulomb integral of the methylated carbon atom is altered in magnitude. This perturbation will be referred to as the inductive effect. It will bring about a shift in all the orbital energies of the molecule, the energy of the ith M.O. being changed from ε_i to ε_i'. The relation between these two quantities can be expressed as a Taylor series involving $\delta\alpha_r$, the change in the Coulomb integral of the methylated atom, *viz.*

$$\varepsilon_i' = \varepsilon_i + \frac{\partial \varepsilon_i}{\partial \alpha_r} \cdot \delta\alpha_r + \tfrac{1}{2} \frac{\partial^2 \varepsilon_i}{\partial \alpha_r^2} (\delta\alpha_r)^2 + \ldots . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Using the well-known relationships

$$\frac{\partial \varepsilon_i}{\partial \alpha_r} = c_{ir}^2; \quad \frac{\partial^2 \varepsilon_i}{\partial \alpha_r^2} = 2 \sum_{j(\neq i)} \frac{c_{ir}^2 \, c_{jr}^2}{\varepsilon_i - \varepsilon_j}$$

(Coulson and Longuet-Higgins, *loc. cit*), where c_{ir} denotes the atomic orbital coefficient of the rth atom in the ith M.O. and neglecting terms higher than $(\delta\alpha_r)^2$, we have

$$\varepsilon_i' = \varepsilon_i + c_{ir}^2\delta\alpha_r + \sum_{j(\neq i)} \frac{c_{ir}^2\, c_{jr}^2}{\varepsilon_i - \varepsilon_j}(\delta\alpha_r)^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Hence, if the suffixes a and b refer respectively to the highest bonding M.O. and the lowest antibonding M.O. of the unperturbed hydrocarbon, it readily follows that the net change in energy of the $N \longrightarrow V_1$ transition due to the inductive effect of the alkyl group is, by equation (2),

$$\begin{aligned}(\Delta\varepsilon_{ab})_{\text{inductive}} &\equiv (\varepsilon_b' - \varepsilon_a') - (\varepsilon_b - \varepsilon_a) = (\varepsilon_b' - \varepsilon_b) - (\varepsilon_a' - \varepsilon_a) \\ &= (c^2_{br} - c^2_{ar})\,\delta\alpha_r + \left(\sum_{j(\neq b)} \frac{c_{br}^2\, c_{jr}^2}{\varepsilon_b - \varepsilon_j} - \sum_{j(\neq a)} \frac{c_{ar}^2\, c_{jr}^2}{\varepsilon_a - \varepsilon_j}\right)(\delta\alpha_r)^2 \quad . \quad . \quad (3)\end{aligned}$$

The Hyperconjugation Effect.—Regarding the molecule and the methyl group as two separate conjugated systems, one may consider how the orbitals of the two systems will change when they are joined, and the consequent change in the energy of the $N \longrightarrow V_1$ transition. If this hyperconjugation effect is small, it is legitimate to regard the orbitals ψ_a' and ψ_b' of the linked system as perturbed forms of the corresponding orbitals ψ_a and ψ_b in the original hydrocarbon. As before, let r be the methylated carbon atom in the hydrocarbon R, and let s be the carbon atom of the methyl group S. If β_{rs} is the resonance integral of the resulting bond, then the energy of the ith orbital changes from ε_i to ε_i', where

$$\varepsilon_i' = \varepsilon_i + \frac{\partial\varepsilon_i}{\partial\beta_{rs}} \cdot \beta_{rs} + \tfrac{1}{2}\frac{\partial^2\varepsilon_i}{\partial\beta_{rs}^2} \cdot \beta_{rs}^2 + \ldots . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Now the second term on the right is a first-order perturbation term, and may be written as $\int\psi_i H'\psi_i$, where H' is the perturbation of the Hamiltonian brought about by hyperconjugation. An integral of the form $\int\psi_i H'\psi_k$ is zero unless i refers to R and k to S, or *vice versa*. This is because the only non-vanishing element of the type $\int\phi_p H'\phi_q$ (where the ϕ's denote atomic orbitals of atoms p and q respectively) is $\int\phi_r H'\phi_s = \beta_{rs}$. Therefore if i refers to a M.O. of R, the third term on the right of (4), which is a second-order perturbtion term, may be written as

$$\tfrac{1}{2}\frac{\partial^2\varepsilon_i}{\partial\beta_{rs}^2} \cdot \beta_{rs}^2 = \sum_{k(\neq i)} \frac{(\int\psi_i H'\psi_k)^2}{\varepsilon_i - \varepsilon_k} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

the summation being taken over the M.O.s of S alone. Employing expansions of the type $\psi_i = \sum_p c_{ip}\phi_p$, and using the fact that $\int\phi_r H'\phi_s$ is the only non-vanishing element of its type, we can convert (5) into

$$\tfrac{1}{2}\frac{\partial^2\varepsilon_i}{\partial\beta_{rs}^2} \cdot \beta_{rs}^2 = \sum_{k(\neq i)} \frac{c_{ir}^2\, c_{ks}^2}{\varepsilon_i - \varepsilon_k} \cdot \beta_{rs}^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Hence, from equation (4),

$$\varepsilon_i' = \varepsilon_i + \sum_{k(\neq i)} \frac{c_{ir}^2\, c_{ks}^2}{\varepsilon_i - \varepsilon_k} \cdot \beta_{rs}^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

so that

$$(\Delta\varepsilon_{ab})_{\text{hyperconjugation}} = \beta_{rs}^2 \left(\sum_{k(\neq b)} \frac{c_{br}^2\, c_{ks}^2}{\varepsilon_b - \varepsilon_k} - \sum_{k(\neq a)} \frac{c_{ar}^2\, c_{ks}^2}{\varepsilon_a - \varepsilon_k}\right) \quad . \quad . \quad . \quad (8)$$

where $(\Delta\varepsilon_{ab})_{\text{hyperconjugation}}$ is defined in a similar way to $(\Delta\varepsilon_{ab})_{\text{inductive}}$.

Combination of Effects.—It can be seen on examination that the first cross term between the inductive and hyperconjugation effects, namely, $\frac{\partial^2\varepsilon_i}{\partial\alpha_r\partial\beta_{rs}} \cdot \delta\alpha_r \cdot \beta_{rs}$, is zero, and hence the procedure of merely adding the separate effects is justified in this approximation. We

conclude, therefore, that the total second-order change in the energy of the $N \longrightarrow V_1$ transition is given by

$$(\Delta\varepsilon_{ab})_{\text{total}} = (\Delta\varepsilon_{ab})_{\text{inductive}} + (\Delta\varepsilon_{ab})_{\text{hyperconjugation}}$$

$$= (c_{br}^2 - c_{ar}^2)\delta\alpha_r + \left(\sum_{j(\neq b)} \frac{c_{br}^2\, c_{jr}^2}{\varepsilon_b - \varepsilon_j} - \sum_{j(\neq a)} \frac{c_{ar}^2\, c_{jr}^2}{\varepsilon_a - \varepsilon_j}\right)(\delta\alpha_r)^2$$

$$+ \left(\sum_{k(\neq b)} \frac{c_{br}^2\, c_{ks}^2}{\varepsilon_b - \varepsilon_k} - \sum_{k(\neq a)} \frac{c_{ar}^2\, c_{ks}^2}{\varepsilon_a - \varepsilon_k}\right)\beta_{rs}^2 \quad . \quad . \quad . \quad (9)$$

The two generalisations cited earlier may now be explained in terms of equation (9), it being borne in mind that the term in $(\delta\alpha_r)^2$ is small compared with the other two terms. For alternant hydrocarbons, $c_{ar}^2 = c_{br}^2$ (Coulson and Rushbrooke, *Proc. Camb. Phil. Soc.*, 1940, **36**, 193), so the inductive term in $\delta\alpha_r$ vanishes, and the hyperconjugation term governs the situation. It is now required to show that this hyperconjugation term is of necessity negative.

According to Mulliken *et al.* (*J. Amer. Chem. Soc.*, 1941, **63**, 41), a conjugating methyl group may be regarded as analogous to —C≡N, and written as —C≡H_3. After allowance for the fact that the Coulomb integral of the H_3 group is less than that of the C atom, solution of the secular equation gives two M.O., ψ_1 and ψ_2, with energies ε_1 and ε_2 where $\varepsilon_1 < -\varepsilon_2$. The hyperconjugation term of (9) is in this case seen to be given by

$$\beta_{rs}^2\, c_{ar}^2\left\{c_{1s}^2\left(\frac{1}{\varepsilon_b - \varepsilon_1} - \frac{1}{\varepsilon_a - \varepsilon_1}\right) + c_{2s}^2\left(\frac{1}{\varepsilon_b - \varepsilon_2} - \frac{1}{\varepsilon_a - \varepsilon_2}\right)\right\} \quad . \quad (10)$$

where c_{1s}, c_{2s} are the atomic orbital (A.O.) coefficients for the carbon atom in ψ_1 and ψ_2.

If
$$\varepsilon_1 < \varepsilon_a < 0 < \varepsilon_b < \varepsilon_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10a)$$

this expression will always be negative. Now for C≡H_3, ε_1 and $-\varepsilon_2$ are both approximately equal to 2β. For unsaturated hydrocarbons, on the other hand, ε_a and $-\varepsilon_b$ are fractions of β, so that the above inequalities hold, and $(\Delta\varepsilon_{ab})_{\text{hyperconjugation}} < 0$. In alternant hydrocarbons, therefore, the shift is always bathochromic.

For non-alternant hydrocarbons, the hyperconjugation term may be written

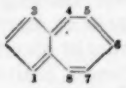
$$(\Delta\varepsilon_{ab})_{\text{hyperconjugation}} = \beta_{rs}^2\left\{c_{br}^2\left(\frac{c_{1s}^2}{\varepsilon_b - \varepsilon_1} + \frac{c_{2s}^2}{\varepsilon_b - \varepsilon_2}\right) - c_{ar}^2\left(\frac{c_{1s}^2}{\varepsilon_a - \varepsilon_1} + \frac{c_{2s}^2}{\varepsilon_a - \varepsilon_2}\right)\right\} \quad . \quad (11)$$

By assuming $\varepsilon_1 = -\varepsilon_2$, and the inequalities (10*a*), it is seen that $(\Delta\varepsilon_{ab})_{\text{hyperconjugation}} < 0$ in all cases, and this is the condition for a bathochromic shift. [The assumption $\varepsilon_1 = -\varepsilon_2$ implies equal Coulomb integrals for the C and H_3 orbitals of the methyl group; this assumption, though perhaps not exactly correct (see above), is almost certainly adequate for determining the sign of $(\Delta\varepsilon_{ab})_{\text{hyperconjugation}}$.]

The essential difference, according to this treatment, between alternant and non-alternant hydrocarbons is that in the latter, the term in $\delta\alpha_r$ does not vanish. Indeed, if $c_{br}^2 > c_{ar}^2$, this term will by itself tend to produce a hypsochromic shift, since, for alkyl substitution, $\delta\alpha_r$ is positive. Hence, alkyl substitution in non-alternant hydrocarbons may produce either bathochromic or hypsochromic shifts—perhaps shifts of opposite sense by substitution at different positions—according to the geometry of the molecule. If $c_{br}^2 < c_{ar}^2$ it can be seen at once that a hypsochromic shift will not be produced by substitution at atom *r*.

Application to Methylated Azulene and Fulvene.—As has already been mentioned, theoretical work by Pullman *et al.* on azulene and its methylated derivatives has led in all cases to a qualitative agreement with the spectral shift observed on methylation. The approximate method described above has been applied to the same molecules, the value of $\delta\alpha_r$ being taken to be $-0{\cdot}1\beta$, that of β_{rs} to be $0{\cdot}7\beta$, the resonance integral of C≡H_3 to be 2β, and the Coulomb integral of H_3 to be $\alpha - 0{\cdot}2\beta$, where β is the resonance integral of the carbon–carbon bond, and α is the Coulomb integral of the carbon atom, all these values

being those employed by Pullman. The correction to the resonance integral of the binuclear bond, introduced in Pullman's work, has not been applied here. The calculated changes in energy of the $N \longrightarrow V_1$ transitions are as given in the table, the atoms being numbered as in (I), and they are seen, on the whole, to compare well with those obtained



(I)

(II)

by exact solution of the secular equations.[1] What is more important, the results agree qualitatively with experimental observation, predicting a bathochomic shift at positions 3 and 5, and a hypsochromic one at positions 2, 4, and 6. For fulvene, numbered as in (II), application of the approximate method leads to the prediction of a hypsochromic shift on substitution at position 1 in accordance with the predictions of Pullman *et al.* (*J. Chem. Physics*, 1950, **18**, 257).

Position of Me group	$N \longrightarrow V_1$ change (in β units) calculated: approximately	by soln. of secular eqns.
2	0·0056	0·0080
3	−0·0547	−0·0525
4	0·0088	0·0075
5	−0·0156	−0·0234
6	0·0148	0·0172

Extension to Dimethyl Derivatives.—Sõrm and Knessel (*Coll. Czech. Chem. Comm.*, 1949, **14**, 201) have carried out studies on the 2 : 6- and 4 : 6-dimethyl derivatives of azulene, and have measured the hypsochromic shifts produced in the $N \longrightarrow V_1$ peak by dimethyl substitution. In the following table, these observed values are compared with those obtained by calculation, the effects of methyl substitution being assumed to be additive. The experimental data for the 2-, 4-, and 6-monomethylazulenes are taken from Plattner and Heilbronner (*Helv. Chim. Acta*, 1947, **30**, 910).

Hypsochromic shifts (mμ) *in* $N \longrightarrow V_1$ *peak in methyl-substituted azulenes.*

2-Me, obs.	6-Me, obs.	2 : 6-Me_2, calc.	2 : 6-Me_2, obs.	4-Me, obs.	6-Me, obs.	4 : 6-Me_2, calc.	4 : 6-Me_2, obs.
−21	−16	−37	−37	−17	−16	−33	−35

The observed additivity is interpreted as follows. Since the inductive effect, as we have represented it, is a first-order perturbation at the position of substitution, this effect will be additive for two or more substituents. Accordingly, we need only consider the effect of hyperconjugation. If perturbation of the ith orbital is brought about by substitution of two methyl groups in the molecule, equation (4) becomes

$$\varepsilon_i' = \varepsilon_i + \frac{\partial \varepsilon_i}{\partial \beta_1} \cdot \beta_1 + \frac{\partial \varepsilon_i}{\partial \beta_2} \cdot \beta_2 + \frac{\partial^2 \varepsilon_i}{\partial \beta_1^2} (\beta_1)^2 + \frac{\partial^2 \varepsilon_i}{\partial \beta_2^2} (\beta_2)^2 + \frac{\partial^2 \varepsilon_i}{\partial \beta_1 \partial \beta_2} \cdot \beta_1 \beta_2 + \ldots . \quad (12)$$

where the suffixes 1 and 2 refer to the two groups. It is seen that additivity of the hyperconjugation effect is conditioned by whether or not the cross term $\frac{\partial^2 \varepsilon_i}{\partial \beta_1 \partial \beta_2} \cdot \beta_1 \beta_2$ vanishes.

The fact that the cross-term does vanish becomes apparent if the expansion is written in the form

$$\varepsilon_i' = \varepsilon_i + \int \psi_i H' \psi_i + \sum_{(\neq i)} \frac{(\int \psi_i H' \psi_j)^2}{\varepsilon_i - \varepsilon_j} + \ldots . \quad (13)$$

Here ψ_i is an orbital of the unsubstituted system, and ψ_j is an orbital of one or other of the entering methyl groups. Hence each term in the sum must contain either β_1 or β_2, but not both : the cross term is therefore zero.

Reduction Potentials.—According to Maccoll (*Nature*, 1949, **162**, 178), the heat of

reduction ΔH of a conjugated molecule may be taken as the energy required to place one or two electrons in the lowest unoccupied orbital, which is, in the ground state, the lowest antibonding orbital. If this is correct, any change in the energy of this orbital should be reflected in a change in the value of ΔH. From the calculations described above, it is found that the A.O. coefficient c_{ar} of the highest bonding orbital in azulene is zero at positions 2 and 6, and that this coefficient is zero at position 1 of fulvene. Thus, by equation (9), any change in $N \longrightarrow V_1$ energy brought about by methyl substitution at these positions is due to displacement of the lowest antibonding orbital. Hence the hypsochromic shifts caused by substitution of various groups at these positions would be expected to run parallel to the changes brought about in the heat of reduction.

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THE UNIVERSITY, MANCHESTER, 13. [*Received, November 12th,* 1951.]

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257. *The* iso*Propylidene Derivatives of Hexahydric Alcohols. Part II.** iso*Propylidene Derivatives of Sorbitol.*

By E. J. BOURNE, G. P. MCSWEENEY, M. STACEY, and L. F. WIGGINS.

Graded acidic hydrolysis of tri*iso*propylidene sorbitol is shown to give 3 : 4-5 : 6-di*iso*propylidene sorbitol, 3 : 4-*iso*propylidene sorbitol, and sorbitol. This proves the triketal to be 1 : 2-3 : 4-5 : 6-tri*iso*propylidene sorbitol. Some new derivatives of 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-D-arabinose are described.

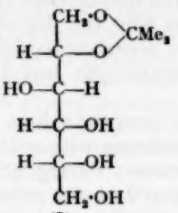
THE early claim by Speier (*Ber.*, 1895, **28**, 2531) that a crystalline tri*iso*propylidene sorbitol results from the condensation of sorbitol (D-glucitol) with excess of acetone in the presence of 1% hydrogen chloride has since been verified by Asahina and Shinoda (*J. Pharm. Soc. Japan*, 1930, **50**, 1; *Chem. Abs.*, 1930, **24**, 1704) and by Strain (*J. Amer. Chem. Soc.*, 1934, **56**, 1756). Recently, Pressman, Anderson, and Lardy (*ibid.*, 1950, **72**, 2404) reported that they had prepared the 1 : 2- (I) and the 1 : 2-5 : 6-*iso*propylidene derivative (II) by treating sorbitol with acetone in the presence of zinc chloride, and had converted the di*iso*propylidene compound into tri*iso*propylidene sorbitol with acetone and concentrated sulphuric acid. This evidence did not permit a precise structure to be assigned to the triketal because of the possibility of rearrangement of the *iso*propylidene groups in the presence of concentrated sulphuric acid. We have now proved that tri*iso*propylidene sorbitol possesses the 1 : 2-3 : 4-5 : 6-structure (III) by showing that it can be converted, by partial acidic hydrolysis, into 3 : 4-5 : 6-di*iso*propylidene sorbitol (V) and 3 : 4-*iso*propylidene sorbitol (VI), compounds which were not encountered by Pressman, Anderson, and Lardy (*loc. cit.*).

After tri*iso*propylidene sorbitol had been submitted to mild acid hydrolysis, the products were separated, by fractional crystallisation and fractional distillation, into unchanged tri*iso*propylidene sorbitol (46%), a crystalline di*iso*propylidene sorbitol (10%), a syrupy mixture (A) of di*iso*propylidene sorbitols (14%), and a crystalline mono*iso*propylidene sorbitol (8%). The two new crystalline compounds were shown to be derivatives of sorbitol by conversion into tri*iso*propylidene sorbitol and sorbitol hexa-acetate, this step being necessary because they had been prepared in small yields from a sorbitol sample which had not been specially purified (cf. Bourne and Wiggins, *J.*, 1948, 1933; Barker and Bourne, *J.*, 1952, 905).

The crystalline mono*iso*propylidene sorbitol gave syrupy tetramethyl, tetra-acetyl, and tetramethanesulphonyl derivatives. Acidic hydrolysis of the tetramethyl ether yielded a syrupy tetramethyl hexitol; this syrup rapidly consumed one mol. of lead tetra-acetate, and so must have possessed an α-glycol group. It followed that a five-membered ketal ring must

* Part I, *J.*, 1946, 13.

have been present in the *iso*propylidene sorbitol and, since this compound readily formed crystalline dityryl and diacetyl dityryl derivatives, it was probable that the ring did not involve either of the primary positions of the hexitol molecule (cf. Helferich, *Adv. Carbohydrate Chem.*, 1948, **3**, 88); thus the *iso*propylidene group most probably engaged the 2 : 3-, 3 : 4-, or 4 : 5-positions. The second of these three possibilities would have explained why the tetramethanesulphonyl ester of the *iso*propylidene sorbitol yielded iodine and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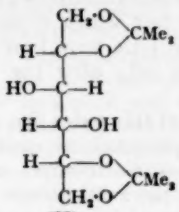
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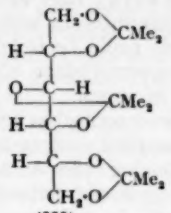
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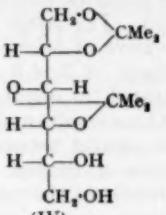
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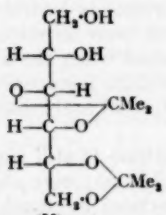
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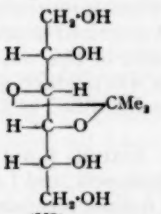
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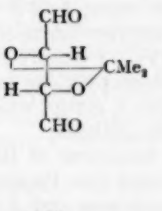
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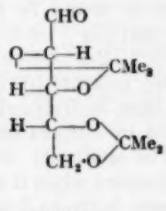
(VIII)

3·3 mols. of sodium methanesulphonate when heated with sodium iodide in acetone at 100°, for in this case the methanesulphonyloxy-groups would have been arranged in vicinal pairs at the primary and adjacent secondary positions (cf. Bladon and Owen, *J.*, 1950, 598). Nevertheless, in view of the fact that 3 : 4-dimethanesulphonyl 1 : 2-5 : 6-di*iso*propylidene mannitol undergoes the same exchange reaction (Bladon and Owen, *loc. cit.*), this conversion could not be used as a basis for the unequivocal elimination of the alternative 2 : 3- and 4 : 5-structures.

Proof that the *iso*propylidene sorbitol was in fact the 3 : 4-compound (VI) was obtained from a completely independent approach, namely, from an examination of its behaviour when treated with sodium metaperiodate. The consumption of 1·93 mols. resulted in the production of 2 mols. of formaldehyde, but no formic acid. In conformity with this conclusion, the larger fragment resulting from the oxidation was identified as 2 : 3-*iso*propylidene D-*threo*dihydroxysuccindialdehyde (VII) by conversion into 2 : 3-*iso*propylidene D-*threo*dihydroxysuccindialdehyde bisphenylhydrazone and dibenzylidene D-threitol, both known compounds.

The structure of the crystalline di*iso*propylidene sorbitol was established in a similar manner. Since the compound rapidly consumed 0·99 mol. of sodium metaperiodate and gave 0·86 mol. of formaldehyde, it must have carried an α-glycol group at either the 1 : 2- or the 5 : 6-position. In the former case the major oxidation product should have been a di*iso*propylidene *aldehydo*-D-arabinose and, in the latter, a di*iso*propylidene *aldehydo*-L-xylose. A syrupy di*iso*propylidene pentose was isolated and had physical constants similar to those reported by Wiggins (*J.*, 1946, 13) and by English and Griswold (*J. Amer. Chem. Soc.*, 1948, **70**, 1390) for 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-D-arabinose (VIII). Moreover, D-arabinose dibenzyl mercaptal and α-D-arabinose tetra-acetate were isolated when the product of the hydrolysis of the syrup was treated with the appropriate reagents. Thus the crystalline di*iso*propylidene sorbitol must have been one of the three possible isomers possessing the 3 : 4 : 5 : 6-structure. The fact that its ditoluene-*p*-sulphonate gave iodine and 1·84 mols. of sodium toluene-*p*-sulphonate, when treated with sodium iodide in acetone at 100°, was in agreement with this view.

The definite assignment of the 3 : 4-5 : 6-structure (V) to the crystalline di*iso*propyl-

idene sorbitol became possible when it was converted into the above 3 : 4-*iso*propylidene sorbitol by acidic hydrolysis. It followed that the triketal from which both were derived initially was 1 : 2-3 : 4-5 : 6-tri*iso*propylidene sorbitol (III) and that the di*iso*propylidene *aldehydo*-D-arabinose aforementioned carried the acetone residues in the 2 : 3- and the 4 : 5-positions (VIII).

Two new crystalline derivatives of 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-D-arabinose were prepared during this work; they were the semicarbazone and the bisdimedone compound. The latter was insoluble in water, a fact which explained why the dimedone derivative of formaldehyde could be isolated in pure form from the periodate oxidation products of 3 : 4-5 : 6-di*iso*propylidene sorbitol only after the formaldehyde had been separated by distillation in steam.

These results and those described in Part I of this series (*loc. cit.*) show that there is a close parallel between mannitol and sorbitol inasmuch as each condenses with acetone to give a triketal possessing the 1 : 2-3 : 4-5 : 6-structure; moreover, during acidic hydrolysis of the tri*iso*propylidene derivatives, the ketal groups engaged at the primary positions are the least stable in each case. One might expect that two di*iso*propylidene sorbitols would be formed when 1 : 2-3 : 4-5 : 6-tri*iso*propylidene sorbitol is hydrolysed, *i.e.*, that the 3 : 4-5 : 6-di*iso*propylidene sorbitol described should have been accompanied by its 1 : 2-3 : 4-isomer (IV). Evidence in support of this was obtained when the above syrupy mixture (A) of di*iso*propylidene sorbitols was oxidised with sodium metaperiodate and then hydrolysed to give a syrup, which was identified as a mixture of arabinose and xylose by chromatographic analysis.

The similarity of the behaviour of the two hexitols towards acetone is still further emphasised when it is recalled that Pressman, Anderson, and Lardy (*loc. cit.*) were able to prepare both 1 : 2-*iso*propylidene and 1 : 2- 5 : 6-di*iso*propylidene sorbitol by much the same procedure as Baer and Fischer (*J. Biol. Chem.*, 1939, **128**, 463) used to prepare 1 : 2-5 : 6-di*iso*propylidene mannitol.

Experimental

1 : 2-3 : 4-5 : 6-*Tri*iso*propylidene Sorbitol from Sorbitol.*—A mixture of sorbitol (80 g.), acetone (1 l.), and concentrated sulphuric acid (8 c.c.) was shaken for 18 hours, neutralised with concentrated aqueous ammonia (*d* 0·880; 28 c.c.) and sodium carbonate (50 g.), and filtered. The filtrate and acetone washings were combined, concentrated at 12 mm., in the presence of a small amount of sodium carbonate, to *ca.* 150 c.c., and poured into ice-water (2·5 l.). Recrystallisation of the precipitate, from aqueous acetone containing a trace of ammonia, gave colourless needles of tri*iso*propylidene sorbitol (51·2 g.), m. p. 46°, $[\alpha]_D^{18}$ +13·8° (*c*, 6·1 in methyl alcohol); reported constants are m. p. 45—48°, $[\alpha]_D$ +12·7°, +14·3° (in ethyl alcohol) (Asahina and Shinoda, *loc. cit.*; Strain, *loc. cit.*; Pressman, Anderson, and Lardy, *loc. cit.*).

Graded Hydrolysis of 1 : 2-3 : 4-5 : 6-*Tri*iso*propylidene Sorbitol.*—A solution of tri*iso*propylidene sorbitol (32·3 g.) in absolute ethyl alcohol (792 c.c.), containing 5N-hydrochloric acid (16·2 c.c.), was kept at 18—20° for 105 minutes, cooled to 0°, neutralised with barium carbonate, and filtered. The filtrate and alcohol washings were combined and evaporated at 40°, leaving a syrup, which was extracted exhaustively with cold acetone. Evaporation of the acetone solution gave a syrup, which was dissolved in ethyl alcohol (30 c.c.) and poured into ice-water containing a trace of ammonia. Recrystallised from aqueous acetone, the precipitate gave tri*iso*propylidene sorbitol (15 g.), m. p. 45° alone or on admixture with the above specimen.

Evaporation of the aqueous alcoholic solution yielded a syrup, which was extracted exhaustively with cold benzene, leaving a solid residue; several crystallisations of the solid from dry acetone gave 3 : 4-iso*propylidene sorbitol* (2·0 g.), m. p. 89—90°, $[\alpha]_D^{20}$ +31·0°(*c*, 4·9 in methyl alcohol) (Found: C, 48·8; H, 8·0. $C_9H_{18}O_6$ requires C, 48·6; H, 8·2%).

The benzene solution was evaporated and the residue was distilled at 0·015 mm., a fraction which had b. p. 138° (bath-temp.) being collected as a colourless syrup (6·6 g.), having n_D^{16} 1·4650 (Found: C, 55·0; H, 8·3. Calc. for $C_{12}H_{22}O_6$: C, 55·0; H, 8·5%). Crystallisation of this fraction from ether–light petroleum (b. p. 40—60°) gave 3 : 4-5 : 6-*di*iso*propylidene sorbitol* (2·8 g.), m. p. 55—56°, $[\alpha]_D^{19}$ +25·2° (*c*, 1·4 in ethyl alcohol). This compound gave correct analytical data for a hemihydrate, even after being dried at 25°/0·01 mm. over phosphoric anhydride [Found (on samples from three separate experiments): C, 53·0, 52·9, 53·0; H, 8·4,

8·7, 8·5. $C_{12}H_{22}O_6,\frac{1}{2}H_2O$ requires C, 53·1; H, 8·5%]. A syrupy residue (A) resulted from evaporation of the ether–light petroleum mother-liquors; its examination is reported on p. 1414.

1 : 2-3 : 4-5 : 6-*Tri*iso*propylidene Sorbitol from* 3 : 4-iso*Propylidene Sorbitol*.—**3 : 4-*iso*-**Propylidene sorbitol (1·0 g.), condensed with acetone, as described above, yielded **1 : 2-3 : 4-5 : 6-tri*iso*propylidene sorbitol (0·55 g.), m. p. 46° alone or on admixture with a specimen prepared directly from sorbitol.

1 : 2-3 : 4-5 : 6-*Tri*iso*propylidene Sorbitol from* 3 : 4-5 : 6-*Di*iso*propylidene Sorbitol*.—Treatment of **3 : 4-5 : 6-di*iso*propylidene sorbitol (0·50 g.) with acetone and concentrated sulphuric acid, as described above, gave **1 : 2-3 : 4-5 : 6-tri*iso*propylidene sorbitol (0·29 g.), m. p. 45—46° alone or on admixture with a specimen prepared directly from sorbitol.

Sorbitol Hexa-acetate from **3 : 4-iso*Propylidene Sorbitol*.**—The *iso*propylidene compound (0·30 g.) was heated at 100° for 2 hours with N-sulphuric acid (5 c.c.). The solution was diluted with water (20 c.c.), neutralised with barium carbonate, filtered, and concentrated to a syrup, which, when acetylated, gave sorbitol hexa-acetate (0·35 g.), m. p. and mixed m. p. 99—100°.

Sorbitol Hexa-acetate from **3 : 4-5 : 6-*Di*iso*propylidene Sorbitol*.**—When hydrolysed and then acetylated (see above), **3 : 4-5 : 6-di*iso*propylidene sorbitol (0·30 g.) gave sorbitol hexa-acetate (0·25 g.), m. p. and mixed m. p. 100°.

1 : 2 : 5 : 6-*Tetra-acetyl* 3 : 4-iso*Propylidene Sorbitol*.—A mixture of **3 : 4-*iso*-**propylidene sorbitol (1·00 g.), acetic anhydride (2·7 c.c.), and pyridine (15 c.c.) was kept at 25° for three days, poured into excess of sodium hydrogen carbonate solution, and extracted with chloroform. The extracts were washed successively with dilute sulphuric acid, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), filtered, and concentrated to a syrup, which was then distilled. The main fraction (1·32 g.) of the *tetra-acetate* had b. p. 160—164° (bath-temp.)/0·04 mm., $[\alpha]_D^{20}$ +8·0° (*c*, 2·3 in chloroform), n_D^{19} 1·4475 (Found: C, 52·5; H, 6·7; Ac, 44·2. $C_{17}H_{26}O_{10}$ requires C, 52·3; H, 6·7; Ac, 44·1%).

1 : 2 : 5 : 6-*Tetramethanesulphonyl* 3 : 4-iso*Propylidene Sorbitol*.—A solution of **3 : 4-*iso*-**propylidene sorbitol (0·50 g.) and methanesulphonyl chloride (4 mols.) in dry pyridine (4·0 c.c.) was kept at 0° for 20 hours, poured into water (30 c.c.), and extracted with chloroform. The extracts were washed successively with ice-cold dilute sulphuric acid, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), filtered, and evaporated at 30°, leaving a syrup, which was dried at 30°/0·01 mm. to give **1 : 2 : 5 : 6-*tetramethanesulphonyl* 3 : 4-iso*propylidene sorbitol* (1·08 g.) as a glass, $[\alpha]_D^{18}$ −2·7° (*c*, 3·7 in chloroform) (Found: C, 28·9; H, 5·0; S, 24·5. $C_{13}H_{26}O_{14}S_4$ requires C, 29·2; H, 4·9; S, 24·0%).

Treatment of **1 : 2 : 5 : 6-*Tetramethanesulphonyl* 3 : 4-iso*Propylidene Sorbitol with Sodium Iodide*.**—The methanesulphonate (1·068 g.) was heated in a sealed tube with sodium iodide (1·30 g.) and dry acetone (15 c.c.) for 4 hours at 100°, during which an intense iodine colour developed. The resulting precipitate was collected, washed with acetone (45 c.c.), and dried at 100°, to give sodium methanesulphonate (0·776 g., representing an exchange of 3·28 methanesulphonyloxy-groups per molecule of the ketal).

1 : 2 : 5 : 6-*Tetramethyl* 3 : 4-iso*Propylidene Sorbitol*.—An anhydrous solution of **3 : 4-*iso*-**propylidene sorbitol (2·00 g.) in acetone (10 c.c.) was refluxed for 20 hours with methyl iodide (5 c.c.) and silver oxide (10 g.). The solvents were removed by distillation and the residue was extracted exhaustively with hot chloroform. The methylation was repeated twice with acetone as the solvent and twice without acetone. The final syrup was distilled at 90—110° (bath-temp.)/0·2 mm. and then refractionated. The bulk of the product distilled at 90—92° (bath-temp.)/0·015 mm., giving the *tetramethyl ether* as a colourless, mobile syrup (0·90 g.), $[\alpha]_D^{17}$ +23·7° (*c*, 1·3 in methyl alcohol), n_D^{17} 1·4425 (Found: C, 55·8; H, 9·1. $C_{13}H_{26}O_6$ requires C, 56·1; H, 9·4%).

1 : 2 : 5 : 6-*Tetramethyl Sorbitol*.—A solution of **1 : 2 : 5 : 6-**tetramethyl **3 : 4-*iso*-**propylidene sorbitol (0·66 g.) in methyl alcohol (24·5 c.c.) and 5N-hydrochloric acid (0·5 c.c.) was kept at 18° for 26 hours, neutralised with silver carbonate, and filtered. The filtrate and methanolic washings were combined and concentrated, the colloidal silver which separated being removed by filtration through "Celite." Complete removal of the solvent left a syrup, which was fractionally distilled at 0·015 mm. The main fraction, a colourless, mobile syrup (0·46 g.), b. p. 113—120° (bath-temp.)/0·015 mm., $[\alpha]_D^{16}$ −4·0° (*c*, 5·5 in methyl alcohol), n_D^{22} 1·4540, was the *tetramethyl sorbitol* (Found: C, 50·3; H, 9·0. $C_{10}H_{22}O_6$ requires C, 50·4; H, 9·3%).

Treatment of **1 : 2 : 5 : 6-*Tetramethyl Sorbitol with Lead Tetra-acetate*.**—The tetramethyl sorbitol (0·0486 g.) was oxidised with lead tetra-acetate in glacial acetic acid, and the excess of the oxidising agent was determined by Hockett and McClenahan's method (*J. Amer. Chem. Soc.*, 1939, **61**, 1667). The number of moles of lead tetra-acetate consumed per mole of tetra-

methyl sorbitol was: 1·03 (2 minutes), 1·06 (9 minutes), 1·06 (46 minutes), 1·11 (71 minutes), and 1·16 (325 minutes).

3 : 4-iso*Propylidene* 1 : 6-*Dirityl Sorbitol*.—A solution of triphenylmethyl chloride (1·20 g.) and **3 : 4-*iso*propylidene** sorbitol (0·50 g.) in dry pyridine (4·0 c.c.) was kept at room temperature for 24 hours and poured into ice-water (90 c.c.). The resulting oil was separated by decantation, washed with cold aqueous alcohol, and then crystallised from aqueous alcohol, to give **3 : 4-iso*propylidene* 1 : 6-*dirityl sorbitol hydrate*** (0·80 g.) as small prisms, m. p. 79—83°, $[\alpha]_D^{20}$ +1·0° (*c*, 2·2 in pyridine) (Found: C, 78·0; H, 6·9. $C_{47}H_{46}O_6,H_2O$ requires C, 77·9; H, 6·7%).

2 : 5-*Diacetyl* 3 : 4-iso*Propylidene* 1 : 6-*Dirityl Sorbitol*.—A solution of triphenylmethyl chloride (1·20 g.) and **3 : 4-*iso*propylidene** sorbitol (0·50 g.) in dry pyridine (10 c.c.) was kept at room temperature for 36 hours before acetic anhydride (0·50 c.c.) was added. After another 48 hours, the solution was poured into ice-water (70 c.c.) giving a white precipitate, which, when crystallised from ethyl alcohol, afforded **2 : 5-*diacetyl* 3 : 4-iso*propylidene* 1 : 6-*dirityl sorbitol*** (1·30 g.), m. p. 103—105°, $[\alpha]_D^{17}$ +6·6° (*c*, 2·4 in pyridine) (Found: C, 77·7; H, 6·4. $C_{51}H_{50}O_6$ requires C, 77·5; H, 6·4%).

Oxidation of **3 : 4-iso*Propylidene Sorbitol with Sodium Metaperiodate*.**—(a) *Amount of periodate consumed.* An aqueous solution of **3 : 4-*iso*propylidene** sorbitol (0·050 g.) was mixed with 0·28M-sodium metaperiodate (10 c.c.), and the whole was diluted to 50 c.c. The sorbitol derivative was omitted from a similar control solution. Portions (2 c.c.) of the reaction mixture and of the control solution were withdrawn at intervals; each portion was added immediately to a solution of sodium hydrogen carbonate (0·50 g.) and potassium iodide (1·0 g.) in water (50 c.c.), and the iodine liberated was titrated against sodium arsenite solution (cf. Jackson, *Org. Reactions*, 1944, **2**, 341). From the results, the number of moles of periodate consumed per mole of **3 : 4-*iso*propylidene** sorbitol was calculated to be: 1·82 (2 minutes), 1·88 (4 minutes), 1·93 (63 minutes), and 1·93 (36 hours).

(b) *Determination of formic acid produced.* To **3 : 4-*iso*propylidene** sorbitol (0·0146 g.) in water (15 c.c.), 0·25M-sodium metaperiodate (10 c.c.) was added and the mixture was kept at 20° for 1 hour (cf. Hirst and Jones, *J.*, 1949, 1659). A portion (5 c.c.) of the solution was mixed with ethylene glycol (0·2 c.c.) to destroy excess of periodate and titrated against 0·01N-sodium hydroxide, methyl-red being used as the indicator. No formic acid was produced, because the slightly acid solution required the same volume of alkali for neutralisation as did a control from which the *iso*propylidene sorbitol was omitted.

(c) *Determination of formaldehyde produced.* **3 : 4-*iso*Propylidene** sorbitol ($1·2 \times 10^{-4}$ mole) was oxidised with sodium metaperiodate and the formaldehyde produced was isolated as its dimedone derivative (m. p. 188°), as described by Reeves (*J. Amer. Chem. Soc.*, 1941, **63**, 1476). Two independent experiments showed, respectively, 1·94 and 2·00 moles of formaldehyde to be liberated from each mole of **3 : 4-*iso*propylidene** sorbitol.

2 : 3-iso*Propylidene* D-threo*Dihydroxysuccindialdehyde*.—An aqueous solution (35 c.c.) of **3 : 4-*iso*propylidene** sorbitol (4·00 g.) and sodium metaperiodate (2 mols.) was kept at room temperature for 20 hours, before being evaporated at 12 mm. in the presence of sodium hydrogen carbonate. The residue was extracted exhaustively with chloroform and the dried extracts were evaporated to give a syrup (2·58 g.), which was dried at 40°/0·01 mm. and was essentially **2 : 3-*iso*propylidene D-*threo*dihydroxysuccindialdehyde**.

A solution of the dialdehyde (0·20 g.) in ethyl alcohol (5 c.c.) was heated for 90 minutes with phenylhydrazine (0·30 g.), and then water was added until a faint turbidity was produced. On cooling, buff-coloured needles (0·11 g.) of the phenylhydrazone were deposited. Recrystallised twice from ethyl alcohol, they had m. p. 143°, $[\alpha]_D^{14}$ −236° (*c*, 0·9 in chloroform). Fischer and Appel (*Helv. Chim. Acta*, 1934, **17**, 1574) gave m. p. 145°, $[\alpha]_D^{20}$ −239° (in ethyl alcohol), for this compound.

***Dibenzylidene* D-*Threitol*.**—A solution of **2 : 3-*iso*propylidene D-*threo*dihydroxysuccindialdehyde** (1·0 g.) in N-sulphuric acid (8 c.c.) was kept at 100° for 3 hours, neutralised with barium carbonate, and centrifuged. The supernatant liquid was evaporated at 35°; an aqueous solution (20 c.c.) of the residue was stirred with sodium amalgam for 5 hours, neutralised with sulphuric acid, and evaporated at 12 mm., the residue being extracted with hot dry methyl alcohol. The extract was concentrated to 25 c.c., saturated with dry hydrogen chloride, shaken for 20 hours with benzaldehyde (10 c.c.), neutralised with sodium hydrogen carbonate, and filtered. The filtrate and methanolic washings were concentrated at 12 mm.; water was added during the distillation to aid the removal of the excess of benzaldehyde. The syrup which was extracted with chloroform from the residue was crystallised thrice from ethyl alcohol and once from dioxan, to give dibenzylidene D-threitol, m. p. 228°, alone or on admixture with

a specimen prepared from 3 : 4-*cyclo*hexylidene D-mannitol (Bourne, Corbett, and Erilinne, *J.*, 1950, 786).

3 : 4-5 : 6-*Diiso*propylidene 1 : 2-*Ditoluene*-p-*sulphonyl Sorbitol*.—A solution of 3 : 4-5 : 6-di*iso*propylidene sorbitol (0·40 g.) and toluene-*p*-sulphonyl chloride (0·64 g.) in dry pyridine (2 c.c.) was kept at room temperature for 20 hours, poured into ice-water (120 c.c.), and extracted with chloroform. The extracts were washed successively with ice-cold dilute sulphuric acid, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), filtered, and evaporated to a syrupy *ester* (0·65 g.), which was dried at 30°/0·01 mm.; it had $[\alpha]_D^{20}$ +11·8° (*c*, 4·4 in chloroform) (Found : C, 54·4; H, 6·1; S, 11·1. $C_{26}H_{34}O_{10}S_2$ requires C, 54·7; H, 6·0; S, 11·2%).

Treatment of 3 : 4-5 : 6-*Diiso*propylidene 1 : 2-*Ditoluene*-p-*sulphonyl Sorbitol with Sodium Iodide*.—The ditoluene-*p*-sulphonate (0·5867 g.) was heated in a sealed tube at 100° for 6 hours with sodium iodide (0·70 g.) and dry acetone (15 c.c.), an intense iodine colour developing. The precipitated sodium toluene-*p*-sulphonate, after being washed with dry acetone (15 c.c.) and dried at 100°, weighed 0·3646 g., which represented an exchange of 1·84 toluene-*p*-sulphonyloxy-groups per molecule of the diketal.

Oxidation of 3 : 4-5 : 6-*Diiso*propylidene *Sorbitol with Sodium Metaperiodate*.—(a) *Amount of periodate consumed*. A solution (35 c.c.) of 3 : 4-5 : 6-di*iso*propylidene sorbitol (0·0478 g.) in water was mixed with 0·3M-sodium metaperiodate (5 c.c.), and the whole was diluted to 50 c.c. The excess of periodate was determined at intervals by the method already described. The number of moles of periodate consumed per mole of di*iso*propylidene sorbitol was : 0·93 (2 minutes), 0·96 (5 minutes), 0·99 (10 minutes), and 0·99 (30 minutes).

(b) *Determination of formaldehyde produced*. (i) 3 : 4-5 : 6-Di*iso*propylidene sorbitol (0·0333 g.) was oxidised with sodium metaperiodate and an attempt was made to isolate the resulting formaldehyde as its dimedone derivative, according to Reeves's method (*loc. cit.*). However, the product (0·0788 g.), which corresponded in weight to 2·1 moles of formaldehyde per mole of di*iso*propylidene sorbitol, had m. p. 136—162°, compared with m. p. 189° for the dimedone derivative of formaldehyde; it was most probably a mixture of the water-insoluble dimedone derivatives of formaldehyde and 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-D-arabinose (see later).

(ii) An aqueous solution (2·0 c.c.) of the di*iso*propylidene sorbitol (0·0144 g.) was mixed with 0·1M-sodium metaperiodate (5·0 c.c.), kept at room temperature for 2 hours, and distilled in steam under diminished pressure. The distillate, treated with a solution of dimedone in ethyl alcohol, gave 0·86 mol. of the dimedone derivative of formaldehyde, m. p. and mixed m. p. 187—188°.

2 : 3-4 : 5-*Diiso*propylidene aldehydo-D-*Arabinose*.—A solution of sodium metaperiodate (3·10 g.) and 3 : 4-5 : 6-di*iso*propylidene sorbitol (3·10 g.) in water (40 c.c.) was kept at room temperature for 5 hours, saturated with sodium chloride, and extracted exhaustively with chloroform. The extracts were dried ($MgSO_4$), filtered, and evaporated to a syrup, which was fractionally distilled. The major fraction was a mobile syrup (2·1 g.), which had b. p. 85—90° (bath-temp.)/0·04 mm., $[\alpha]_D^{17}$ −17·1° (*c*, 7·2 in chloroform), n_D^{16} 1·4480. Wiggins (*loc. cit.*) gave b. p. 80° (bath-temp.)/0·03 mm., $[\alpha]_D^{17}$ −14·4° (in chloroform), n_D^{23} 1·4421, for 2 : 3-4 : 5-di-*iso*propylidene *aldehydo*-D-arabinose; English and Griswold (*loc. cit.*) recorded b. p. 60—65°/0·08 mm., $[\alpha]_D^{22}$ −18·2° (in chloroform).

D-*Arabinose Dibenzyl Mercaptal*.—The di*iso*propylidene *aldehydo*-D-arabinose (0·10 g.) was shaken with toluene-ω-thiol (0·20 g.) and concentrated hydrochloric acid (0·10 c.c.) for 9 hours. Ice-water was added, giving an oil; addition of ether extracted the excess of thiol and left a white solid, which was recrystallised from absolute ethyl alcohol, to yield silky needles of D-arabinose dibenzyl mercaptal (0·05 g.), $[\alpha]_D^{13}$ +19·0° (*c*, 2·8 in pyridine), m. p. 148—149° alone or on admixture with an authentic specimen (Found : C, 60·0; H, 6·2; S, 16·7. Calc. for $C_{19}H_{24}O_4S_2$: C, 60·0; H, 6·35; S, 16·85%).

α-D-*Arabinose Tetra-acetate*.—A solution of di*iso*propylidene *aldehydo*-D-arabinose (1·0 g.) in N-sulphuric acid (10 c.c.) was kept at 100° for 1 hour, neutralised with barium carbonate, and filtered. The filtrate and aqueous washings were combined and evaporated at 12 mm. to a syrup (0·50 g.). Examination by filter-paper chromatography showed arabinose to be the only sugar component. The syrup was treated with acetic anhydride (2·5 c.c.) and fused sodium acetate (0·4 g.) at 100° for 1 hour, cooled, and poured into water, from which the ester was extracted with chloroform. The syrupy product had partly crystallised after several days. The crystals, separated by trituration with aqueous ethyl alcohol, had m. p. 94° alone or on admixture with an authentic specimen of α-D-arabinose tetra-acetate, and showed $[\alpha]_D^{19}$ −41·2° (*c*, 3·2 in chloroform).

Bisdimedone Derivative of 2 : 3-4 : 5-*Diisopropylidene* aldehydo-D-*Arabinose*.—A solution of dimedone (0·72 g.) in 50% aqueous alcohol (16 c.c.) was added to a solution of 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-D-arabinose (0·20 g.) in the same solvent (5 c.c.), and the mixture was kept at room temperature for 40 hours before being heated to 70° for 2 hours. Water (10 c.c.) was added and the solution cooled. Recrystallised twice from aqueous ethyl alcohol, the precipitate gave stout prisms of the *bisdimedone* derivative (0·30 g.), m. p. 147—148°, depressed on admixture with dimedone itself, $[\alpha]_D^{19}$ −34·8° (*c*, 2·7 in chloroform) (Found: C, 66·0; H, 8·0. $C_{27}H_{40}O_8$ requires C, 65·8; H, 8·2%).

2 : 3-4 : 5-*Diisopropylidene* aldehydo-D-*Arabinose Semicarbazone*.—Di*iso*propylidene *aldehydo*-D-arabinose (0·20 g.) was treated with an aqueous solution (0·5 c.c.) of sodium acetate (0·3 g.) and semicarbazide hydrochloride (0·20 g.). After 24 hours, water (3 c.c.) was added; the precipitate, crystallised from benzene–light petroleum (b. p. 60—80°), gave needles of 2 : 3-4 : 5-*diisopropylidene* aldehydo-D-*arabinose semicarbazone*, m. p. 144—145°, $[\alpha]_D^{16}$ +7·6° (*c*, 2·9 in ethyl alcohol) (Found: C, 50·2; H, 7·3; N, 14·6. $C_{12}H_{21}O_5N_3$ requires C, 50·2; H, 7·4; N, 14·6%).

3 : 4-iso*Propylidene Sorbitol from* 3 : 4-5 : 6-*Diisopropylidene Sorbitol*.—A solution of 3 : 4-5 : 6-di*iso*propylidene sorbitol (1·253 g.) in ethyl alcohol (28·3 c.c.) and N-hydrochloric acid (3·1 c.c.) was kept at 19·5° for 49 minutes, cooled to 0°, neutralised with lead carbonate, and filtered. The filtrate and alcohol washings were combined and evaporated to a syrup, which was extracted with acetone. The syrup obtained when the extracts were evaporated was stirred with hot benzene and then allowed to cool. Recrystallisation of the solid product from acetone gave 3 : 4-*iso*propylidene sorbitol (0·36 g.), m. p. 89—90°, alone or on admixture with the sample described above.

Examination of the Syrupy Mixture (*A*) *of Diisopropylidene Sorbitols*.—The syrup (A) (p. 1411) was treated with sodium metaperiodate, and the resulting mixture of pentose derivatives was hydrolysed, under conditions similar to those already described for the conversion of 3 : 4-5 : 6-di*iso*propylidene sorbitol into D-arabinose. An aqueous solution (3%) of the syrupy product was analysed by filter-paper chromatography, the developing solvent being the upper phase of a mixture of butanol (40%), ethanol (10%), water (49%), and ammonia (1%) (Partridge, *Nature*, 1946, **158**, 270). An aniline hydrogen phthalate spray revealed two components; these had R_F values identical with those of xylose and arabinose, used as standards on the same chromatogram.

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258. *Studies in the Polyene Series. Part XLII.* Some Reactions of* cyclo*Hexenyl-lithium with Polyene Aldehydes.*

By E. A. BRAUDE, T. BRUUN, B. C. L. WEEDON, and R. J. WOODS.

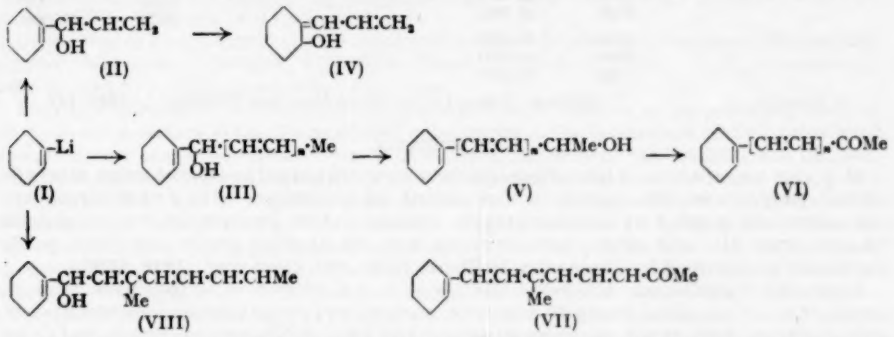
The application of *cyclo*hexenyl-lithium to the preparation of some intermediates for the synthesis of vitamin A analogues has been examined.

*cyclo*Hexenyl-lithium reacts with sorbaldehyde, octatrienal, and 3-methyloctatrienal to give the carbinols (III; $n = 2$ and 3) and (VIII) respectively. Anionotropic rearrangement of (III; $n = 2$ and 3) and oxidation of the resulting isomers give the triene ketone (VI; $n = 2$) and a tetraene ketone, probably (VI; $n = 3$), respectively. Attempts to convert (VIII) into the ketone (VII) were unsuccessful.

IN exploring the scope of application of alkenyl-lithium reagents it was demonstrated (Braude and Coles, *J.*, 1950, 2014) that *cyclo*hexenyl-lithium (I) is readily prepared and reacts with acraldehyde and crotonaldehyde, yielding the carbinols (II) and (III; $n = 1$) respectively, and further that these undergo anionotropic rearrangement to (IV) and

* Part XLI, *J.*, 1952, 1154.

(V; $n = 1$), respectively. The last on oxidation yielded the corresponding ketone (VI; $n = 1$), previously obtained by a number of alternative routes (Heilbron, Jones, Richardson, and Sondheimer, *J.*, 1949, 737; Chanley and Sobotka, *J. Amer. Chem. Soc.*, 1949, **71**, 4141). To account for the difference in direction of rearrangement of the carbinols (II) and (III; $n = 1$) it was suggested that the hydroxyl group migrates initially to the γ-carbon atom at which electron accession is greatest. Other factors, such as the strain accompanying the formation of an exocyclic double bond, may also be involved, but are of less importance (Braude and Forbes, *J.*, 1951, 1755). These observations suggested that the reaction of *cyclo*hexenyl-lithium (I) with polyene aldehydes, substituted in such a manner as to favour isomerisation of the resulting carbinols to *cyclo*hexenyl rather than to *cyclo*hexylidene derivatives, might furnish routes to polyene ketones of use for the synthesis of compounds related to vitamin A. This paper reports an investigation of these possibilities by using the polyene aldehydes, sorbaldehyde, octatrienal, and 3-methyloctatrienal.

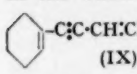


Addition of sorbaldehyde to an ethereal solution of (I) furnished the carbinol (III; $n = 2$), in yields up to 67% (based on aldehyde). The carbinol was characterised by oxidation to the corresponding ketone (2 : 4-dinitrophenylhydrazone), and by catalytic hydrogenation and subsequent oxidation to 1-*cyclo*hexylhexan-1-one. Dilute hydrochloric acid rearranged (III; $n = 2$) to a product which was similarly converted into the known 6-*cyclo*hexylhexan-2-one (semicarbazone) by hydrogenation and subsequent oxidation. None of the isomeric 2-*n*-hexyl*cyclo*hexanone (a sample of which was prepared by alkylation of *cyclo*hexanone) could be detected, and it was therefore concluded that isomerisation of (III; $n = 2$) gives mainly, if not exclusively, (V; $n = 2$) by migration of the hydroxyl group along the side chain as in the case of the carbinol from crotonaldehyde. Oxidation of the rearranged product with aluminium *tert.*-butoxide and acetone yielded the triene ketone (VI; $n = 2$), the structure of which was confirmed by hydrogenation to 6-*cyclo*hexylhexan-2-one.

Attempts were next made to carry out similar series of reactions with the triene aldehydes, octa-2 : 4 : 6-trien-1-al and 3-methylocta-2 : 4 : 6-trien-1-al. The expected product (VII) from the latter would be of particular interest as a possible intermediate for the synthesis of a compound possessing the polyene side chain of vitamin A but a modified ring system (cf. Weedon and Woods, *J.*, 1951, 2687). The carbinols (III; $n = 3$) and (VIII) were obtained in good yields, the latter being characterised by oxidation to the corresponding ketone (2 : 4-dinitrophenylhydrazone) and catalytic reduction to 1-*cyclo*hexyl-3-methyloctan-1-ol. The unstable product formed on rearrangement of (III; $n = 3$) with dilute acid was estimated by light-absorption measurements to contain a high proportion of a fully conjugated tetraene. This, by analogy, with the carbinols similarly obtained from crotonaldehyde and sorbaldehyde, is formulated as (V; $n = 3$); it yielded a ketone, probably (VI; $n = 3$), which was isolated as its 2 : 4-dinitrophenylhydrazone, the light-absorption properties of the ketone and of its derivative being in agreement with this structure. Treatment of (VIII) with acids, however, gave a mixture of products which, on oxidation, yielded an unidentified carbonyl compound (semicarbazone and

2 : 4-dinitrophenylsemicarbazone) but none of the required tetraene ketone (VII). Since alternative routes to (VII) have now been developed (Bharucha and Weedon, forthcoming publication), investigations along these lines have for the present been discontinued.

Light-absorption data for the majority of the compounds referred to above are collected in the Table. The *cyclo*hexenylcarbinols (III; $n = 2$ and 3), (VIII), and (V; $n = 2$) exhibit maxima of high intensity at wave-lengths consistent with the conjugated diene or triene structures assigned. The triene ketone (VI; $n = 2$) shows maximal absorption at slightly longer wave-lengths, and of higher intensity, than that of the acetylenic analogue (IX).



(IX)

	$\lambda_{max.}$, Å	$\varepsilon_{max.}$		$\lambda_{max.}$, Å	$\varepsilon_{max.}$
(III; $n = 2$)	2280	25 000	(VIII)	2690	41 000
	2350 *	23 000		2780	38 500
(V; $n = 2$)	2590 *	25 000	(VI; $n = 2$)	3200	37 500
	2700	33 500	(IX) †	2220	7 500
	2790	27 500		3120	20 000
(III; $n = 3$)	2590 *	32 500			
	2690	44 000			
	2780	34 500			

* Inflexion. † Heilbron, Jones, Lewis, Richardson, and Weedon, *J.*, 1949, 742.

Experimental

M. p.s are uncorrected. Light-absorption data were determined in ethanol unless otherwise stated. Wherever possible, operations were carried out in nitrogen. The 2 : 4-dinitrophenylhydrazones were purified by chromatographic adsorption from benzene solution on alumina (Spence, grade H). All other chromatograms were on alumina which had been partly deactivated as described by Cheeseman, Heilbron, Jones, and Weedon (*J.*, 1949, 2310).

1-cyclo*Hex*-1′-*enylhexa*-2 : 4-*dien*-1-*ol* (III; $n = 2$).—A solution of sorbaldehyde (15·5 g.) in ether (40 c.c.) was added during 20 minutes to a stirred and cooled (ice–salt) solution of *cyclo*hexenyl-lithium (from 18·8 g. of chloro*cyclo*hexene and 2·3 g. of lithium; cf. Braude and Coles, *J.*, 1950, 2014) in ether (310 c.c.). The mixture was stirred for a further hour at 0° and the temperature then allowed to rise to 20°. Ice and water were added and the product was extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4 and a trace of K_2CO_3), and evaporated. Distillation of the residue from a short-path still was accompanied by extensive polymerisation and gave 1-cyclo*hex*-1′-*enylhexa*-2 : 4-*dien*-1-*ol* (12·5 g., 44%), b. p. 60° (bath-temp.)/10^{-4} mm., n_D^{16} 1·5358 (Found: C, 80·8; H, 10·15. $C_{12}H_{18}O$ requires C, 80·9; H, 10·2%). Light absorption: see Table.

Repetition of the preceding experiment with twice the quantity of *cyclo*hexenyl-lithium and distillation of the crude product in batches of about 10 g. raised the yield of carbinol to 67%.

1-cyclo*Hexylhexan*-1-*ol and* 1-cyclo*Hexylhexan*-1-*one*.—A solution of the preceding carbinol (900 mg.) in methanol (25 c.c.) was shaken in hydrogen in the presence of platinic oxide (90 mg.) until absorption was complete (2·8 mols.). After removal of catalyst and solvent, the residue was distilled, giving the saturated *carbinol* (600 mg.), b. p. 40—50° (bath-temp.)/10^{-4} mm., n_D^{16} 1·4740 (Found: C, 78·4; H, 13·0. $C_{12}H_{24}O$ requires C, 78·2; H, 13·15%).

This product (785 mg.) in acetone (1·1 c.c.) was oxidised with a solution of chromium trioxide (332 mg.) and concentrated sulphuric acid (0·3 c.c.) in water (1·1 c.c.). The crude product (770 mg.) was isolated in the usual way. One portion (25 mg.) was converted into the 2 : 4-*dinitrophenylsemicarbazone* (32 mg.), which crystallised for alcohol–chloroform in yellow leaflets, m. p. 189° (Found: C, 56·3; H, 6·65; N, 17·4. $C_{19}H_{27}O_5N_5$ requires C, 56·25; H, 6·7; N, 17·25%). A second portion (740 mg.) was heated on the steam-bath for 1½ hours with an excess of methanolic semicarbazide acetate and gave the *semicarbazone* (126 mg.), which crystallised from methanol in laths, m. p. 136° (Found: C, 65·25; H, 10·6; N, 17·7. $C_{13}H_{25}ON_3$ requires C, 65·25; H, 10·55; N, 17·55%). Light absorption: maximum, 2280 Å; ε, 15 000.

1-cyclo*Hex*-1′-*enylhexa*-2 : 4-*dien*-1-*one*.—A solution of 1-*cyclo*hex-1′-enylhexa-2 : 4-dien-1-ol 1·53 g.) and aluminium *tert.*-butoxide (5 g.) in acetone (83 c.c.) and benzene (124 c.c.) was heated under reflux for 48 hours. The mixture was cooled and then shaken with dilute sulphuric acid (670 c.c.; 2·5% w/v). The benzene layer was separated, washed with water, dried, and evaporated. Distillation of the residue gave the crude ketone (1·1 g.), b. p. 50° (bath-temp.)/10^{-4} mm., n_D^{21} 1·5584. Light absorption: maximum, 2940 Å; $E_{1\,cm.}^{1\%}$, 820. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in red needles, m. p. 232° (Found: N, 15·6.

$C_{18}H_{20}O_4N_4$ requires N, 15·7%). Light absorption in chloroform (main band only): maximum, 3980 Å; ε, 37 500.

A portion (0·8 g.) of the crude ketone in light petroleum (b. p. 40—60°) was poured on to a column of alumina. Elution of the main band with the same solvent and distillation gave 1-cyclo*Hex*-1′-*enylhexa*-2 : 4-*dien*-1-*one* (600 mg.), b. p. 60° (bath-temp.)/10^{-3} mm., n_D^{21} 1·5632, which solidified when kept at 0° but melted again on warming to 20° (Found: C, 81·9; H, 9·25. $C_{12}H_{16}O$ requires C, 81·75; H, 9·15%). Light absorption: maximum, 2930 Å; ε, 19 500.

A solution of the preceding ketone (500 mg.) in ethyl acetate (10 c.c.) was shaken in hydrogen in the presence of platinic oxide until absorption was complete (2·8 mols.). After removal of catalyst and solvent, the residue was converted into the semicarbazone which had m. p. 136°, undepressed on admixture with the specimen described above.

6-cyclo*Hex*-1′-*enylhexa*-3 : 5-*dien*-2-*ol* (V; $n = 2$).—A solution of 1-*cyclo*hex-1′-enylhexa-2 : 4-dien-1-ol (10 g.) and concentrated hydrochloric acid (0·21 c.c.) in a mixture of water (63 c.c.) and acetone (145 c.c.) was kept at 20° for 18 hours and then diluted with water. The crude product (9 g.) was isolated by means of ether. Light absorption: maxima, 2690 and 2800 Å; $E_{1\,cm.}^{1\%}$, 1680 and 1410 respectively.

Distillation of a small portion of the crude product gave 6-cyclo*hex*-1′-*enylhexa*-3 : 5-*dien*-2-*ol*, b. p. 70° (bath-temp.)/10^{-4} mm., n_D^{18} 1·5668 (Found: C, 81·0; H, 10·0. $C_{12}H_{18}O$ requires C, 80·9; H, 10·2%). Light absorption: see Table.

6-cyclo*Hexylhexan*-2-*ol and* 6-cyclo*Hexylhexan*-2-*one*.—A solution of the preceding carbinol (1·3 g.) in ethyl acetate (15 c.c.) was shaken in hydrogen in the presence of platinic oxide until absorption was complete. After removal of catalyst and solvent, the residue was distilled, giving the saturated carbinol (290 mg.), b. p. 70° (bath-temp.)/10^{-4} mm.

A portion (240 mg.) of the carbinol in acetone (0·35 c.c.) was oxidised with a solution of chromium trioxide (102 mg.) and concentrated sulphuric acid (0·1 c.c.) in water (0·35 c.c.). The crude ketone was isolated in the usual way and treated with an excess of semicarbazide acetate in methanol. The crude derivative was crystallised once from methanol and had m. p. 148—150° (100 mg.). One further crystallisation from the same solvent gave 6-*cyclo*hexylhexan-2-one semicarbazone as plates, m. p. 154°, undepressed on admixture of the sample with an authentic specimen (Heilbron, Jones, Lewis, Richardson, and Weedon, *J.*, 1949, 742, give m. p. 154°).

2-n-*Hexyl*cyclo*hexanone* (with K. R. Bharucha).—A mixture of *cyclo*hexanone (4·9 g.) and *n*-hexyl bromide (8·4 g.) was poured into a boiling solution of potassium *tert.*-butoxide (from 2·2 g. of potassium) in *tert.*-butanol (25 c.c.) (cf. Braude and Coles, *J.*, 1950, 2014). The mixture was heated under reflux for 20 minutes, then cooled and treated with excess of cold (0°) 2N-hydrochloric acid. Isolation of the crude product (9·5 g.) with ether in the usual manner and distillation gave 2-n-*hexyl*cyclo*hexanone* (2·9 g.), b. p. 80—91°/0·5 mm., n_D^{24} 1·4570 (Found: C, 79·05; H, 12·15. $C_{12}H_{22}O$ requires C, 78·65; H, 12·25%). The *semicarbazone* crystallised from methanol in needles, m. p. 128—129° (Found: N, 17·55. $C_{13}H_{25}ON_3$ requires N, 17·85%). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in orange needles, m. p. 130° (Found: N, 15·3. $C_{18}H_{26}O_4N_4$ requires N, 15·45%).

6-cyclo*Hex*-1′-*enylhexa*-3 : 5-*dien*-2-*one* (VI; $n = 2$).—A solution of 6-*cyclo*hex-1′-enylhexa-3 : 5-dien-2-ol (9·1 g.) and aluminium *tert.*-butoxide (30 g.) in a mixture of acetone (500 c.c.) and benzene (750 c.c.) was heated under reflux for 48 hours. The mixture was then cooled and shaken with dilute sulphuric acid (4 l.; 2·5% w/v). The benzene layer was separated, washed with water, dried, and evaporated, giving the crude product (9 g.). Light absorption: maxima, 2800 and 3240 Å; $E_{1\,cm.}^{1\%}$, 580 and 600 respectively.

A portion (7·5 g.) of the crude product in light petroleum (b. p. 40—60°) was poured on to a column of alumina (235 g.; grade IV). The chromatogram was developed with the same solvent and the main yellow band eluted, yielding the crude ketone as an oil (3·4 g.), n_D^{22} 1·5995. Light absoprtion: maximum, 3240 Å; $E_{1\,cm.}^{1\%}$, 1580. The 2 : 4-*dinitrophenylhydrazone* was purified by chromatographic absorption on alumina (only one band being observed) and crystallised from ethyl acetate, giving red leaflets, m. p. 205° (Found: N, 16·0. $C_{18}H_{20}O_4N_4$ requires N, 15·7%). Light absorption in chloroform (main band only): maximum 4120 Å; ε, 38 000.

The crude ketone was treated with a methanolic solution of semicarbazide acetate (from 3·8 g. of semicarbazide hydrochloride), and the mixture kept for 24 hours at 20° and then for 24 hours at 0°. The solid (1·3 g.) which separated was removed and crystallised from methanol, yielding the *semicarbazone* (800 mg.) as yellow leaflets, m. p. 202° (decomp.) (Found: C, 67·0; H, 8·35. $C_{13}H_{19}ON_3$ requires C, 66·9; H, 8·2%). Light absorption: maxima, 3170 and 3320 Å; ε, 58 000 and 49 000 respectively.

A mixture of the finely powdered semicarbazone (500 mg.), light petroleum (b. p. 40—60°; 25 c.c.), and dilute sulphuric acid (25 c.c.; 10% w/v) was stirred vigorously and heated under reflux until nearly all the solid had disappeared. The mixture was cooled and the upper layer was removed, washed with water, dried, and evaporated. Distillation of the residue gave 6-cyclo*hex*-1′-*enylhexa*-3 : 5-*dien*-2-*one* (221 mg.), n_D^{28} 1·62 (Found: C, 81·35; H, 9·2. $C_{12}H_{14}O$ requires C, 81·75; H, 9·15%). Light absorption: see Table.

6-cyclo*Hexylhexan*-2-*one*.—A solution of the preceding regenerated ketone (172 mg.) in ethyl acetate (15 c.c.) was shaken in hydrogen in the presence of platinic oxide (30 mg.) until absorption was complete (hydrogen absorbed: 68 c.c. at 24°/768 mm., equiv. to 2·9 double bonds). The catalyst and solvent were removed and the residue was treated with semicarbazide acetate (270 mg.) in methanol. The crude product (218 mg.) which separated yielded, from methanol, the semicarbazone (115 mg.) of 6-*cyclo*hexylhexan-2-one as plates, m. p. 154°, undepressed on admixture with an authentic specimen.

1-cyclo*Hex*-1′-*enylocta*-2 : 4 : 6-*trien*-1-*ol* (III; $n = 3$).—A solution of octatrienal (7·7 g.; crystalline, freshly prepared) in ether (30 c.c.) was added slowly to a cooled (ice–salt) solution of *cyclo*hexenyl-lithium (from 20 g. of chloro*cyclo*hexene and 2·4 g. of lithium), and the mixture stirred and cooled for 2 hours. The mixture was added to ice and the product isolated with ether in the usual way, giving an oil (10 g.) which exhibited light absorption maxima at 2680 and 2800 Å ($E_{1\text{ cm.}}^{1\%}$, 1450 and 980 respectively). Distillation of a small portion of the crude product gave the *carbinol*, b. p. 90—100° (bath-temp.)/10^{-4} mm., n_D^{18} 1·572 (Found: C, 81·8; H, 10·15. $C_{14}H_{20}O$ requires C, 82·3; H, 9·9%). Light absorption: see Table. When kept at 0°, the carbinol partly solidified and after recrystallisation from pentane had m. p. *ca.* 60°. Light absorption: maxima, 2580, 2680, and 2800 Å; ε, 36,500, 41 000, and 36 500 respectively.

Treatment of the crude carbinol (9·0 g.) for 17 hours at 20° with a 0·01M-solution of hydrochloric acid in a mixture of acetone (170 c.c.) and water (40 c.c.) gave a product which exhibited light absorption maxima at 3040 and 3150 Å ($E_{1\text{ cm.}}^{1\%}$, 1100 and 1020 respectively) and an inflexion at 2800 and 2900 Å ($E_{1\text{ cm.}}^{1\%}$, 580 and 670 respectively), indicating an appreciable content of the rearranged carbinol. Distillation of a small portion gave an oil, b. p. 90—100° (bath-temp.)/10^{-4} mm., n_D^{24} 1·6015, which exhibited light absorption maxima at 3020 and 3160 Å ($E_{1\text{ cm.}}^{1\%}$, 1550 and 1350 respectively). Oppenauer oxidation of the crude, unstable, rearranged carbinol, and separation of the products by chromatography, yielded (*ca.* 20—25%) a ketonic fraction which exhibited a light absorption maximum at 3480 Å ($E_{1\text{ cm.}}^{1\%}$, 1100). Distillation gave an oil, light absorption maximum, 3510 Å ($E_{1\text{ cm.}}^{1\%}$, 1580). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in needles, m. p. 220° (Found: N, 15·15. $C_{20}H_{20}O_4N_4$ requires N, 14·65%). Light absorption in chloroform (main band only): maximum, 4200 Å; ε, 49 000.

1-cyclo*Hex*-1′-*enyl*-3-*methylocta*-2 : 4 : 6-*trien*-1-*ol* (VIII) *and* 1-cyclo*Hexyl*-3-*methyloctan*-1-*ol*.—A solution of 2-methylhepta-1 : 3 : 5-trien-1-al (20 g.) (Weedon and Woods, *J.*, 1951, 2687) in ether (100 c.c.) was added during 45 minutes to a cooled (0°) solution of *cyclo*hexenyl-lithium (from 21·6 g. of chloro*cyclo*hexene and 2·6 g. of lithium) in ether (500 c.c.). The mixture was stirred overnight at 20°, a saturated aqueous ammonium chloride solution (250 c.c.) was then added, and the product was isolated with ether in the usual manner. Distillation yielded the carbinol (18·2 g., 57%), b. p. 70—75° (bath-temp.)/10^{-4} mm., n_D^{19} 1·5830, which gave erratic analytical results. Light absorption: see Table. To characterise the carbinol a portion (1·0 g.) was oxidised by shaking its solution in light petroleum (b. p. 40—60°; 70 c.c.) with manganese dioxide (5 g.) at 20° for 15 hours (cf. *idem*, *loc. cit.*) and the resulting ketone (0·7 g.), b. p. 75° (bath-temp.)/10^{-4} mm., n_D^{25} 1·6020, was converted into the 2 : 4-*dinitrophenylhydrazone*. This crystallised from ethyl acetate and had m. p. 184° (Found: N, 14·15. $C_{21}H_{24}O_4N_4$ requires N, 14·15%). Light absorption in chloroform (main band only): maximum, 4130 Å; ε, 43 500.

A solution of the preceding carbinol (3·5 g.) in methanol (25 c.c.) was shaken in hydrogen in the presence of platinic oxide until absorption was complete (hydrogen absorbed, 1440 c.c. at 23°/765 mm., equiv. to 3·6 double bonds). Removal of the catalyst and solvent and distillation of the residue gave 1-cyclo*hexyl*-3-*methyloctan*-1-*ol* (2·2 g.), b. p. 95° (bath-temp.)/10^{-4} mm., n_D^{25} 1·4708 (Found: C, 79·55; H, 13·2. $C_{15}H_{30}O$ requires C, 79·55; H, 13·35%).

Treatment of the unsaturated carbinol (VIII) for 4 hours at 20° with a 0·002M-solution of sulphuric acid in a mixture of water (180 c.c.) and acetone (420 c.c.) and chromatographic separation of the products gave an oil (40%), n_D^{19} 1·5725, which exhibited light absorption maxima at 3140 and 3220 Å ($E_{1\text{ cm.}}^{1\%}$, 1210 and 1270 respectively). It decomposed on attempted distillation, the distillate showing light absorption of lower intensity than the starting material. Oxidation of the undistilled material in light petroleum (b. p. 40—60°) with manganese dioxide and chromatographic separation of the products gave an oil (60%), b. p. 70° (bath-temp.)/10^{-4}

mm., n_D^{24} 1·6047; light absorption: maxima, 2680, 2790, and 3220 Å; $E_{1\,cm.}^{1\%}$, 1320, 1320, and 1700 respectively. A portion (200 mg.) of the oil was converted into the *semicarbazone* (235 mg.) which crystallised from aqueous methanol in pale yellow needles, m. p. 203° (decomp.) (Found: N, 21·5, 21·45%). Light absorption: maximum, 3300 Å; $E_{1\,cm.}^{1\%}$, 2900. The 2 : 4-*dinitrophenylsemicarbazone* crystallised from aqueous pyridine and had m. p. 218° (decomp.) (Found: N, 19·5%). Light absorption in chloroform: maximum, 3380 Å; $E_{1\,cm.}^{1\%}$, 1450. An attempt to oxidise the crude rearranged carbinol by the Oppenauer method was unsuccessful. Treatment of (VIII) with acids under more vigorous conditions than those described above led to extensive dehydration and decomposition of the product.

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259. *Alkenylation employing Lithium Alkenyls. Part VI.* The Synthesis and Spectral Properties of Some* 6 : 6-*Dimethylcyclohexenyl Derivatives.*

By E. A. BRAUDE, T. BRUUN, B. C. L. WEEDON, and R. J. WOODS.

The method of direct alkenylation has been applied to the synthesis of 6 : 6-dimethyl*cyclo*hexenyl derivatives. 1-Chloro-6 : 6-dimethyl*cyclo*hexene, prepared from 2 : 2-dimethyl*cyclo*hexanone, has been converted into 6 : 6-dimethyl*cyclo*hexenyl-lithium, which with benzaldehyde and benzophenone affords the carbinols (I; R = H and Ph). Under mild acidic conditions, the phenylcarbinol (I; R = H) undergoes rearrangement to the isomer (II; R = H), while the diphenylcarbinol (I; R = Ph) undergoes dehydration to the hydrocarbon (III; R = Ph).

Reaction of the lithium alkenyl with crotonaldehyde and sorbaldehyde, followed by rearrangement, similarly yields the diene and triene carbinols (V; n = 1 and 2) which are selectively oxidised to the ethylenic ketones (VI; n = 1 and 2).

The ultra-violet light-absorption properties of the various conjugated derivatives are recorded and discussed, and provide further striking evidence for the steric effects previously noted for *gem*-dimethyl substituents.

IN two previous papers (Part IV, Braude and Coles, *J.*, 1950, 2014; Braude, Bruun, Weedon, and Woods, *J.*, 1952, 2818) the formation and some synthetic applications of *cyclo*hexenyl-lithium were described. An extension of this work to methylated *cyclo*hexene derivatives was of interest in connection with studies on steric inhibition of resonance in isocyclic systems (cf. *J.*, 1949, 1818), and also in connection with the synthesis of polyenes related to vitamin A (cf. preceding paper). The present communication deals with the preparation and properties of some 6 : 6-dimethyl*cyclo*hexenyl derivatives.

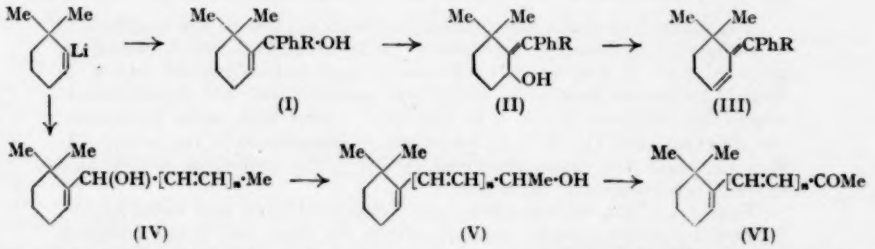
6 : 6-Dimethyl*cyclo*hexenyl-lithium was readily obtained by the action of lithium on 1-chloro-6 : 6-dimethyl*cyclo*hexene. The chloro-compound, together with 1 : 1-dichloro-2 : 2-dimethyl*cyclo*hexane, was prepared by treating 2 : 2-dimethyl*cyclo*hexanone with phosphorus pentachloride. The formation of a mixture of mono- and di-chloro-derivatives was encountered previously with *cyclo*pentanone (Braude and Forbes, *J.*, 1951, 1755), whereas *cyclo*hexanone under similar conditions yielded mainly chloro*cyclo*hexene (Part IV, *loc. cit.*). The by-product in the present instance was obtained as a crystalline solid which was conveniently dehydrochlorinated to the chloro-olefin by means of sodamide in liquid ammonia.

With benzaldehyde, dimethyl*cyclo*hexenyl-lithium affords the crystalline phenylcarbinol (I; R = H) in over 60% yield, and benzophenone similarly gives the diphenylcarbinol (I; R = Ph). On treatment with 0·1M-hydrochloric acid at room temperature, the

* Part V, *J.*, 1951, 2078.

phenylcarbinol is converted smoothly into the conjugated isomer (II; R = H), while the diphenylcarbinol undergoes simultaneous rearrangement and dehydration, yielding only the diene (III; R = Ph). Rearrangement and partial dehydration was also observed in the case of the *cyclo*hexenyl analogue (Part IV, *loc. cit.*), but the occurrence of complete dehydration under such mild conditions is remarkable; it is undoubtedly promoted by the severe steric interference (cf. below) associated with the carbinol (II; R = Ph) which is considerably lessened in the diene (III; R = Ph). The diene (III; R = H) was obtained from the phenylcarbinol (I; R = H) by distillation from potassium hydrogen sulphate.

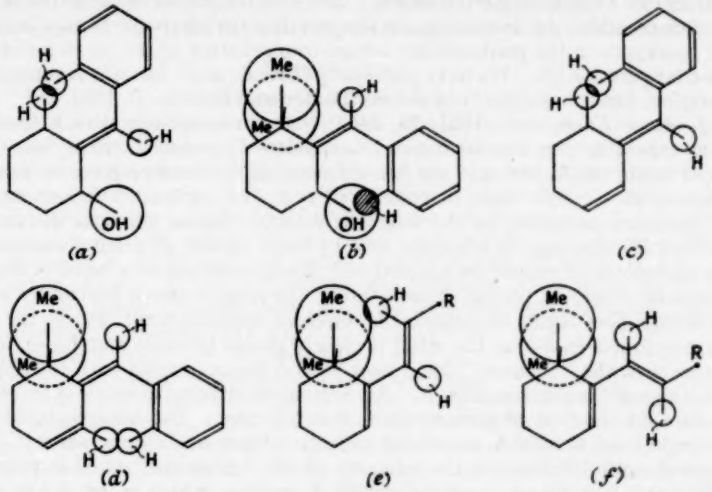
Reaction of the lithium alkenyl with crotonaldehyde gave a 60% yield of the propenylcarbinol (IV; $n = 1$) which, like the *cyclo*hexenyl analogue (Part IV, *loc. cit.*), rearranges, with migration of the hydroxyl group exclusively in the side chain, to the diene carbinol (V; $n = 1$). The constitution of the latter was established by oxidation with acetone and aluminium *tert.*-butoxide or, in superior yield, with manganese dioxide (cf. Weedon and Woods, *J.*, 1951, 2687; Braude and Forbes, *loc. cit.*), to the known diene ketone (VI; $n = 1$) (Heilbron, Jones, Toogood, and Weedon, *J.*, 1949, 2028). From a corresponding reaction with sorbaldehyde, the rearranged triene carbinol (V; $n = 2$) was obtained directly, the initial product (IV; $n = 2$) evidently having undergone isomerisation during isolation. Oxidation of the triene carbinol by the Oppenauer method and separation of the products by chromatography and treatment with the Girard T reagent yielded the triene ketone (VI; $n = 2$).



The ultra-violet light absorption of some of the compounds described above and of their *cyclo*hexenyl or *cyclo*hexylidene analogues are collected in the Table. The wavelength locations of the bands due to the conjugated chromophores are almost identical in the *gem*-dimethyl and in the unsubstituted series, but the intensities are much lower in the former, the ratio (r) of extinction coefficients ranging from 0·71 to 0·42. Analogous observations have previously been made in a number of similar cases (Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890; Braude and Jones, *J. Amer. Chem. Soc.*, 1950, **72**, 1041) and it has been shown that the hypochromic effects can be ascribed to steric inhibition of resonance resulting from the obstruction by the *gem*-dimethyl groups of a coplanar *trans*-arrangement of the conjugated chromophore. A more detailed interpretation of the present results is given in the sequel.

All the compounds listed in the Table are either products of an oxotropic rearrangement, or are derived from such products, and in those cases where stereoisomerism about a double bond is possible the configuration adopted would therefore be expected to be the less sterically hindered one (Braude and Coles, *J.*, 1951, 2085). 2-Benzylidene*cyclo*hexanol would thus be expected to be obtained in configuration (*a*) with the phenyl group on the far side of the hydroxyl substituent (see figure). The scale diagram (in which covalent bond radii have been used) indicates that even in this configuration some interference occurs between hydrogen atoms of the phenyl and the *cyclo*hexane ring and this is borne out by the light absorption which shows a reduction in intensity and hyperchromic shift when compared with the open-chain analogue, methylstyrylcarbinol ($\lambda_{max.}$ 2510 Å, ε 19 500; Braude, Jones, and Stern, *J.*, 1947, 1087). 6-Benzylidene-2 : 2-dimethyl*cyclo*hexanol, on the other hand, presumably adopts the configuration (*b*) since interference between the phenyl and the methyl groups would be even larger than between the phenyl and the hydroxyl groups; the pronounced decrease in $\varepsilon_{max.}$ signifies that, in configuration (*b*), inter-

ference is already considerable and results in an appreciable twisting of the plane of the phenyl ring with respect to that of the ethylenic bond. A similar situation exists in the benzylidene*cyclo*hexenes. The unsubstituted compound, no doubt, is the less hindered, thermodynamically more stable "*trans*"-isomer (*c*) and exhibits absorption similar to that of *trans*-phenylbutadiene ($\lambda_{max.}$ 2800 Å, ε 28 300; Braude, Jones, and Stern, *loc. cit.*). By contrast, the *gem*-dimethyl derivative would be expected to have the *cis*-configuration



(*a*) (*b*) (*c*) (*d*) (*e*) (*f*)

(*d*) corresponding to that of the carbinol from which it is derived, any tendency for isomerisation to the *trans*-isomer to occur being opposed by the strong interference which would result between the phenyl and the methyl groups. The absorption properties are in agreement with this view and closely resemble those of *cis*-phenylbutadiene ($\lambda_{max.}$ 2700 Å, ε 14 000; Grummitt and Christoph, *J. Amer. Chem. Soc.*, 1951, **73**, 3479).

The data for the diphenylmethylene derivatives, in which the possibility of geometrical isomerism does not arise, can be interpreted in an analogous fashion. The absorption of the parent 1 : 1-diphenylethylene ($\lambda_{max.}$ 2500 Å, ε 12 000), unlike that of 1 : 2-diphenylethylene (stilbene), closely resembles that of styrene. The lack of effective conjugation with the second phenyl group may be due to electronic or steric reasons, or both (compare the different spectral relation of Ph·CH=O and $Ph_2C{=}O$, *Ann. Reports*, 1945, **42**, 108); the essential point for the present purpose is that steric interference resulting in the rotation of *one* phenyl ring with respect to the plane of the double bond in the diphenylethylene grouping $Ph_2C{=}C$ will have little effect on the spectral properties. Therefore, diphenylmethylene derivatives, in which the coplanarity of neither or of only one phenyl ring is obstructed by substituents should absorb very similarly to the corresponding benzylidene derivatives, and comparison of the data for 2-benzylidene- and 2-diphenylmethylene-*cyclo*hexanol, 2-benzylidene- and 2-diphenylmethylene-*cyclo*hexene, and 3-benzylidene- and 3-diphenylmethylene-4 : 4-dimethyl*cyclo*hexene (see Table) shows that this is indeed the case. Diphenylmethylene derivatives in which the coplanarity of *both* phenyl rings is obstructed by substituents, on the other hand, should show a very large steric effect and it is interesting that 2-diphenylmethylene-3 : 3-dimethyl*cyclo*hexanol (II; R = Ph) is not formed under the usual conditions, the less hindered dehydration product being obtained instead (see above).

In the *cyclo*hexenyl derivatives, the structural configurations in question are not stereoisomers about a double bond, but *s-cis-trans* about a conventional single bond possessing some double-bond character (*e*, *f*). Whereas the barrier to rotation about a double bond is high (cf. Mulliken and Roothaan, *Chem. Reviews*, 1947, **41**, 219), that for a single bond is quite low (*ca.* 2 kcal.; cf. Aston *et al.*, *J. Chem. Physics*, 1946, **14**, 67) and the two planar

configurations will be in thermal equilibrium at ordinary temperature, the proportion of each depending on their relative free energies. By analogy with butadiene, the unhindered compounds will exist predominantly in the *s-trans*-configuration which will be more stable than the unhindered *s-cis*-configuration by *ca.* 2 kcal. (Aston *et al.*, *loc. cit.*). The configuration of the *gem*-dimethyl derivatives, in which the *s-trans*-form is hindered, will depend on the relative magnitude of the steric effect, which is also expected to be of the order of 2 kcal. although its exact magnitude is unknown. Two interpretations of the hypochromic effects are therefore possible: the decrease in ε in the *gem*-dimethyl derivatives may be due either (i) to steric hindrance in the predominant *s-trans*-configuration (*e*), or (ii) to a change-over to the *s-cis*-configuration (*f*). We have previously (Braude *et al.*, *loc. cit.*) favoured the former interpretation, but it has since been shown (Barton and Brooks, *J.*, 1951, 261; Turner and Voitle, *J. Amer. Chem. Soc.*, 1951, **73**, 1403) that chromophores with a fixed *s-cis*-configuration generally give rise to bands of considerably reduced intensities, even in the absence of steric hindrance, and the second possibility therefore receives some support. Nevertheless, we consider that, in systems of type (VI) at least, the first interpretation remains the more probable, for the following reason. In our previous discussion, it was inferred that the decrease in intensity, due to steric causes, of a band associated with a multiple chromophore should be coupled with the appearance of a band of shorter wavelength associated with a partial chromophore. In most systems previously studied, the partial-chromophore bands lie outside the observed spectral range, but in the case of the 4-*cyclo*hexenylbut-3-en-2-ones the effect is clearly shown (Braude and Jones, *loc. cit.*), the disappearance of the " dienone " band near 2800 Å being coupled with the appearance of a partial " enone " band near 2200 Å. An even more striking example is provided by the present data for the 6-*cyclo*hexenylhexa-3 : 5-dien-2-ones. The unmethylated ketone exhibits a single band at 3200 Å, associated with the " trienone " chromophore $[C{=}C]_3{\cdot}C{=}O$. In the *gem*-dimethyl derivative the intensity of the " trienone " band is reduced to less than half, but a new set of bands near 2700 Å appears, which is, no doubt, due to the partial " dienone " chromophore of the side chain. The appearance of such a well-defined partial-chromophore band would not be expected if the *gem*-dimethyl derivatives (V) and (VI) adopted the unhindered *s-cis* configuration (*f*).*

Ultra-violet light absorptions for ethanol solutions.

	*cyclo*Hexene series		*gem*-Dimethyl*cyclo*hexene series		
	$\lambda_{max.}$, Å	ε	$\lambda_{max.}$, Å	ε	*r* *
2-Benzylidene*cyclo*alkanol (*e.g.*, II; R = H)	2430	14 200 [1]	2370	6700	0·47
3-Benzylidene*cyclo*alkene (*e.g.*, III; R = H)	2810	18 700 [1]	2570	10 000	
			2700	13 000	0·70
			2800	13 000	
2-Diphenylmethylene*cyclo*alkanol	2400	13 200 [1]	—	—	—
3-Diphenylmethylene*cyclo*alkene (*e.g.*, III; R = Ph)	2810	22 000 [1]	2520	15 500	
			2680	15 500	0·71
			2800	15 500	
4-*cyclo*Alkenylbut-3-en-2-ol (*e.g.*, V; *n* = 1)	2350	23 000 [1]	2360	11 000	0·48
4-*cyclo*Alkenylbut-3-en-2-one (*e.g.*, VI; *n* = 1)	2810	20 800 [2]	2810	13 000 [2]	0·62
6-*cyclo*Alkenylhexa-3 : 5-dien-2-ol (*e.g.*, V; *n* = 2)	2700	33 500 [3]	2680	15 000	0·43
			2800	15 000	
6-*cyclo*Alkenylhexa-3 : 5-dien-2-one (*e.g.*, VI; *n* = 2)	3200	37 500 [3]	2680	18 500	
			2800	18 500	
			3260	15 500	0·42 †
			3430	11 500	

* *r* = ε (*gem*-dimethyl series)/ε (unsubstituted series). † Based on 3260-Å band.
[1] Part IV, *loc. cit.* [2] Heilbron *et al.*, *J.*, 1949, 737, 2028; Braude *et al.*, *ibid.*, p. 1890.
[3] Preceding paper.

* *Added in Proof.*—Further evidence has now accumulated in support of this view. Oroshnik, Karmas, and Mebane (*J. Amer. Chem. Soc.*, 1952, **74**, 295) have shown that the abnormal spectral properties of vitamin A and its derivatives also receive a satisfactory interpretation on the basis of steric interference in the *s-trans*-configuration and the concomitant appearance of " partial chromophore " bands. Furthermore, the *X*-ray diffraction analysis of crystalline β-ionylidenecrotonic acid (MacGillavry, Kreuger, and Eichhorn, *Proc. K. Ned. Akad. Wet.*, 1951, *B*, **54**, 449) also indicates an *s-trans*-configuration of the bond joining the substituted *cyclo*hexene ring and the unsaturated side-chain. We are indebted to Professor C. H. MacGillavry, Amsterdam, for an advance copy of her paper.

The steric effects manifested by the spectral data are also reflected in the reduced ease of oxotropic rearrangement in the *gem*-dimethyl*cyclo*hexenyl compared with the *cyclo*hexenyl series. Kinetic measurements, details of which will be reported later, show that the rates of rearrangement of the carbinols (I; R = H) and (IV; $n = 1$) are smaller by factors of about 2 than those of the unsubstituted analogues under identical conditions. These differences are larger than are to be expected from the small electronic influences of the *gem*-dimethyl groups and are undoubtedly to be ascribed, at least in part, to the reduced resonance stabilisation which accompanies the rearrangement in the substituted series.

Experimental

(M. p.s. are uncorrected.)

1-*Chloro*-6 : 6-*dimethyl*cyclo*hexene* *and* 1 : 1-*Dichloro*-2 : 2-*dimethyl*cyclo*hexane*.—2 : 2-Dimethyl*cyclo*hexanone (103 g.) was added dropwise with stirring and cooling (ice-bath) to phosphorus pentachloride (206 g.). Stirring was continued for 1 hour at 20° and the mixture was then added to ice and water (*ca.* 1 l.) and steam-distilled. Isolation of the product from the distillate with ether gave an oil (126 g.), n_D^{20} 1·4800, which was fractionally distilled through a 10" Dufton column, equipped with an efficient reflux head, and gave (i) 1-*chloro*-6 : 6-*dimethyl*cyclo*hexene* (56 g.), b. p. 52°/10 mm., n_D^{23} 1·4731—1·4739 (Found : C, 66·8; H, 9·1; Cl, 24·5. $C_8H_{13}Cl$ requires C, 66·45; H, 9·05; Cl, 24·5%), and (ii) an oil (55 g.), b. p. *ca.* 80°/10 mm., which solidified on cooling. Recrystallisation of the solid from aqueous alcohol gave 1 : 1-*dichloro*-2 : 2-*dimethyl*cyclo*hexane* (26·5 g.), m. p. 123° (Found : C, 53·1; H, 8·25; Cl, 39·3. $C_8H_{14}Cl_2$ requires C, 53·05; H, 7·8; Cl, 39·15%).

To a solution of the above dichloride (13·3 g.) in a mixture of liquid ammonia (75 ml.) and ether (50 ml.), a solution of sodamide (prepared from 1·85 g. of sodium according to Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120) in liquid ammonia (50 ml.) was added slowly. The mixture was stirred for 3 hours, ammonium chloride (5 g.) was then added to decompose the excess of sodamide, and the solvents were evaporated. Isolation of the product with ether and distillation gave (i) 1-chloro-6 : 6-dimethyl*cyclo*hexene (6·3 g.), b. p. 58—60°/14 mm., n_D^{21} 1·4770—1·4781 (Found : C, 67·05; H, 8·75; Cl, 24·65. Calc. for $C_8H_{13}Cl$: C, 66·45; H, 9·05; Cl, 24·5%), and (ii) unchanged dichloride (1·1 g.).

The freshly prepared monochloride gave no immediate precipitate with alcoholic silver nitrate or with a methanolic solution of 2 : 4-dinitrophenylhydrazine sulphate.

(6 : 6-*Dimethyl*cyclo*hexenyl*)*phenylcarbinol* (I; R = H).—6 : 6-Dimethyl*cyclo*hexenyl-lithium was prepared from 1-chloro-6 : 6-dimethyl*cyclo*hexene (43·5 g.; freshly distilled) and lithium (4·2 g.) in ether (600 ml.) by a procedure similar to that described for the preparation of *cyclo*hexenyl-lithium (Braude and Coles, *J.*, 1950, 2014). After removal of a small amount of unchanged lithium, the ethereal solution was cooled to 0°, a solution of benzaldehyde (23·8 g.) in ether (75 ml.) was added dropwise, and the mixture stirred for 18 hours at 20°. Saturated aqueous ammonium chloride (250 ml.) was then added, and the product isolated in the usual manner, giving the *carbinol* (30·7 g., 63%) which crystallised from pentane in needles, m. p. 73·5° (Found : C, 83·6; H, 9·6. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). Light absorption in ethanol : maxima, 2580 and 2640 Å; ε, 205 and 160 respectively.

2-*Benzylidene*-3 : 3-*dimethyl*cyclo*hexanol* (II; R = H).—A solution of the preceding carbinol (6·0 g.) in a 0·1M-solution of sulphuric acid in a mixture of water (40 ml.) and acetone (160 ml.) was kept at 20° for 48 hours. The solution was then neutralised by the addition of aqueous sodium hydrogen carbonate solution, the bulk of the acetone was removed by distillation under reduced pressure through a Dufton column, and the product was isolated with ether in the usual manner. Distillation gave a viscous oil (5·4 g.), b. p. 70° (bath-temp.)/10^{-4} mm., n_D^{20} 1·5563, which solidified on cooling of its solution in pentane to 0°. Recrystallisation from the same solvent yielded the *carbinol* (3·1 g.) as prisms, m. p. 58·5° (Found : C, 83·55; H, 9·6. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). Light absorption : see Table.

3-*Benzylidene*-4 : 4-*dimethyl*cyclo*hexene*.—A mixture of (6 : 6-dimethyl*cyclo*hexenyl)phenylcarbinol (3·0 g.) and finely powdered potassium hydrogen sulphate (2·0 g.) was heated at 80° for 20 minutes under reduced pressure. The products were distilled at 100° (bath)/10^{-4} mm. The distillate (2·5 g.) was diluted with pentane (3 ml.) and cooled to −30°, the crystalline precipitate of unchanged carbinol (m. p. 72°; 1·1 g.) was filtered off, and the mother-liquors were again distilled, giving the *hydrocarbon* (1·1 g.) as a colourless oil, b. p. 85° (bath)/10^{-4} mm., n_D^{25} 1·5720 (Found : C, 90·2; H, 9·0. $C_{15}H_{18}$ requires C, 90·85; H, 9·15%). Light absorption : see Table.

(6 : 6-*Dimethyl*cyclo*hexenyl*)*diphenylcarbinol* (I; R = Ph).—Benzophenone (6·9 g.) in ether (30 ml.) was added slowly to a solution of 6 : 6-dimethyl*cyclo*hexenyl-lithium (from 6·6 g. of 1-chloro-6 : 6-dimethyl*cyclo*hexene and 0·63 g. of lithium) in ether (120 ml.) at 0° and the whole stirred at 20° for 24 hours. Saturated aqueous ammonium chloride solution (50 ml.) was then added and the ethereal layer was separated and dried. Evaporation of the solvent and distillation of the residue gave (i) unchanged benzophenone (6·0 g.), b. p. 99—107°/0·3 mm., and (ii) the *carbinol* which sublimed at 160° (bath-temp.)/10^{-4} mm., and crystallised from aqueous alcohol in hexagonal prisms (1·51 g., 14%), m. p. 95·5° (Found: C, 86·4; H, 8·25. $C_{21}H_{24}O$ requires C, 86·25; H, 8·25%). Light absorption: maximum, 2580 Å; ε, 290. The yield quoted is based on a single experiment and could no doubt be raised considerably.

3-*Diphenylmethylene*-4 : 4-*dimethyl*cyclo*hexene* (III; R = Ph).—A solution of (6 : 6-dimethyl*cyclo*hexenyl)diphenylcarbinol (800 mg.) in a 0·1M-solution of hydrochloric acid in a mixture of water (6 ml.) and acetone (24 ml.) was kept at 20° for 20 hours. Neutralisation of the mixture, removal of the acetone, and isolation of the product in the usual manner gave the *hydrocarbon* (368 mg.) which crystallised from aqueous ethanol in needles, m. p. 63—64° (Found: C, 91·5; H, 8·15. $C_{21}H_{22}$ requires C, 91·9; H, 8·1%). Light absorption: see Table. On dilution of the mother-liquors from the crystallisation with water and seeding, a further crop of the hydrocarbon (255 mg.), m. p. 58—62°, was obtained.

1-(6 : 6-*Dimethyl*cyclo*hex*-1-*enyl*)*but*-2-*en*-1-*ol* (IV; *n* = 1).—A solution of crotonaldehyde (4·2 g.) in ether (25 ml.) was added slowly at 0° to a solution of 6 : 6-dimethyl*cyclo*hexenyl-lithium (from 11·5 g. of 1-chloro-6 : 6-dimethyl*cyclo*hexene and 1·1 g. of lithium) in ether (200 ml.). The mixture was stirred at 20° for 15 hours, a saturated aqueous ammonium chloride solution (90 ml.) was added, and the product isolated as usual. Distillation gave the *carbinol* (8·6 g., 60%), b. p. 60—65° (bath-temp.)/10^{-3} mm., n_D^{25} 1·4990 (Found: C, 79·7; H, 11·15. $C_{12}H_{20}O$ requires C, 79·9; H, 11·2%). The carbinol exhibited no light absorption with ε >200 in the region 2200—3000 Å.

4-(6 : 6-*Dimethyl*cyclo*hex*-1-*enyl*)*but*-3-*en*-2-*ol* (V; *n* = 1).—A solution of the preceding carbinol (4·3 g.) in a 0·01M-solution of hydrochloric acid in a mixture of water (40 ml.) and acetone (60 ml.) was kept at 20° for 2 hours. The product was isolated in the usual manner and distilled, giving the *carbinol* (3·35 g.), b. p. 60—65° (bath-temp.)/10^{-3} mm., n_D^{22} 1·5045 (Found: C, 80·1; H, 11·2. $C_{12}H_{20}O$ requires C, 79·9; H, 11·2%). Light absorption: see Table.

4-(6 : 6-*Dimethyl*cyclo*hex*-1-*enyl*)*but*-3-*en*-2-*one* (VI; *n* = 1).—(*a*) A mixture of the preceding carbinol (3·6 g.), aluminium *tert.*-butoxide (11·5 g.), acetone (190 ml.), and benzene (290 ml.) was heated under reflux for 48 hours. The mixture was then cooled and poured into dilute sulphuric acid (2·5% w/v; 1500 ml.). Isolation of the product in the usual way gave the crude ketone (3·8 g.) which was treated with an excess of semicarbazide acetate in methanol. The resulting semicarbazone (2·1 g.) had m. p. 186—187° which was raised to 188°, undepressed on admixture of the sample with an authentic specimen, on crystallisation from methanol (Heilbron, Jones, Toogood, and Weedon, *J.*, 1949, 2028, give m. p. 186—187°).

(*b*) A solution of the preceding carbinol (2·0 g.) in light petroleum (200 ml.; b. p. 40—60°) was shaken with manganese dioxide (20 g.; cf. Weedon and Woods, *J.*, 1951, 2687) at 20° for 3 hours. The mixture was filtered and the filtrate was evaporated. Distillation of the residue gave the ketone (1·51 g.), b. p. 60° (bath-temp.)/10^{-3} mm., n_D^{20} 1·5111. A portion (0·89 g.) of the ketone was converted into the semicarbazone which crystallised from methanol in plates (0·97 g.), m. p. 187—188°, undepressed on admixture of the sample with an authentic specimen. The 2 : 4-dinitrophenylhydrazone gave a single band on chromatography (benzene–alumina) and crystallised from 1 : 1 ethyl acetate–methanol in red needles, m. p. 157°, undepressed on admixture with an authentic specimen (*idem*, *loc. cit.*, give m. p. 154—155°).

6-(6 : 6-*Dimethyl*cyclo*hex*-1-*enyl*)*hexa*-3 : 5-*dien*-2-*ol* (V; *n* = 2).—A solution of sorbaldehyde (26 g.) in ether (75 ml.) was added slowly to a solution of 6 : 6-dimethyl*cyclo*hexenyl-lithium (from 51 g. of 1-chloro-6 : 6-dimethyl*cyclo*hexene and 4·9 g. of lithium) in ether (600 ml.) at 0°. The mixture was stirred overnight at 20°, saturated aqueous ammonium chloride (450 ml.) was then added, and the product isolated in the usual manner. Distillation gave the *carbinol* (14·5 g., 26%), b. p. 80° (bath-temp.)/10^{-4} mm., n_D^{23} 1·5316 (Found: C, 81·8; H, 10·65. $C_{14}H_{22}O$ requires C, 81·5; H, 10·75%). Light absorption: see Table. No change in light absorption was observed after treatment of a small portion of the carbinol for 2 hours at 20° with 0·01M-sulphuric acid in 4 : 1 dioxan–water.

6-(6 : 6-*Dimethyl*cyclo*hex*-1-*enyl*)*hexa*-3 : 5-*diene*-2-*one*.—A mixture of the preceding carbinol (6·5 g.), aluminium *tert.*-butoxide (15·6 g.), acetone (250 ml.), and benzene (500 ml.) was heated under reflux for 60 hours. The mixture was cooled and poured into dilute sulphuric acid (700

ml.). The product was isolated in the usual manner and dissolved in light petroleum (b. p. 40—60°; 20 ml.). The solution was poured on to a column of alumina (350 g.; grade IV; Brockmann and Schodder, *Ber.*, 1941, **74**, 73) and the chromatogram developed with the same solvent. The main yellow band yielded an oil (2·7 g.), n_D^{17} 1·5647, a portion (1·8 g.) of which was treated with Girard T reagent (Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1095). Isolation of the ketonic fraction gave 6-(6 : 6-*dimethylcyclohex*-1-*enyl*)*hexa*-3 : 5-*dien*-2-*one* as an oil (0·58 g.), b. p. 80° (bath-temp.)/10^{-4} mm., n_D^{21} 1·5680 (Found : C, 82·2; H, 9·8. $C_{14}H_{20}O$ requires C, 82·3; H, 9·85%). Light absorption : See Table.

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260. *Alkenylation employing Lithium Alkenyls. Part VII.* The Reaction of* iso*Butenyl-lithium with Ethylenic Ketones.*

By E. A. BRAUDE and J. A. COLES.

*iso*Butenyl-lithium, previously obtained from *iso*butenyl bromide, is also readily formed from the chloride. Its reactions with methyl vinyl ketone, methyl propenyl ketone, and mesityl oxide have been examined and compared with those of the corresponding ethylenic aldehydes.

Di*iso*butenylcarbinol and di*iso*butenylmethylcarbinol, obtained from the reactions of *iso*butenyl-lithium with β-methylcrotonaldehyde and mesityl oxide, respectively, undergo rearrangement with extreme ease in the presence of dilute acids to the isomers (IV) and (VII), and represent the most mobile oxotropic systems yet known. The isomer (IV) has been synthesised by an alternative route.

IN previous papers (Parts I—III, *J.*, 1950, 2000—2014) the conversion of *iso*butenyl bromide into *iso*butenyl-lithium and the addition reactions of the latter with a variety of carbonyl compounds were described. We have now examined the direct metalation of *iso*butenyl chloride and the alkenylation of αβ-ethylenic ketones as well as of β-methylcrotonaldehyde. The object of the work was threefold : (*a*) to establish to what extent the coupling reaction which accompanies alkenylation with *iso*butenyl bromide, but which is not observed in the case of propenyl bromide (Part V, *J.*, 1951, 2078) or *cyclo*alkenyl chlorides (Part IV, *J.*, 1950, 2014; Part VI;* Braude and Forbes, *J.*, 1951, 1755), is caused by the alkenyl moiety or by the halogen or the carbonyl compound, severally, (*b*) to confirm that the alkenylation of αβ-ethylenic ketones, like those of αβ-ethylenic aldehydes previously studied, proceeds normally and is not accompanied by 1 : 4-addition (1 : 4-addition of lithium derivatives to unsaturated ketones had been noted in certain cases, cf. Tucker and Whalley, *J.*, 1949, 50), and (*c*) to synthesise some missing members in the series of dialkenylcarbinols required in investigations on anionotropic systems.

*iso*Butenyl chloride, conveniently prepared from *iso*butaldehyde by treatment with phosphorus pentachloride, followed by dehydrochlorination (Kirrman, *Bull. Soc. chim.*, 1948, **15**, 163), reacts somewhat less readily than the corresponding bromide with lithium in ether. The difference in reactivity of the two halogen derivatives appears to be smaller than is usual in other reactions of this type, but is to be expected in terms of the mechanism previously suggested for the metalation process (Part V, *loc. cit.*) since the carbon–chlorine bond is stronger than the carbon–bromine bond and since its dimensions are less favourable for accommodation on the metal lattice.

The reaction of *iso*butenyl-lithium with methyl vinyl ketone yielded mainly polymeric material together with 2 : 5-dimethylhexa-2 : 4-diene (*ca.* 35%), but none of the expected

* Part VI, preceding paper.

carbinol could be isolated. This is in contrast to the reaction of *iso*butenyl-lithium with acraldehyde (Part II, *loc. cit.*) as well as those of methyl vinyl ketone with Grignard reagents (Cymerman, Heilbron, and Jones, *J.*, 1944, 144; Lebedeva and Shlyakova, *J. Gen. Chem. Russia*, 1949, **19**, 1290), which gave the expected carbinols, although failure has been reported in one instance (Smith and Sprung, *J. Amer. Chem. Soc.*, 1943, **65**, 1276). Moreover, the extent of the coupling reaction, while of the same order as in alkenylations employing *iso*butenyl bromide, is much larger than in the other three cases described in the sequel, in which no diene was isolated, though small amounts may also be formed. From these facts, it may be inferred (*a*) that the extent of coupling, presumably by the reaction RHal + RLi ⟶ RR + LiHal, during the actual metalation is much less in the case of the chloride than of the bromide, as would be expected by analogy with other cases (Ziegler and Colonius, *Annalen*, 1930, **479**, 135), (*b*) that coupling of the lithium alkenyl, once formed, can be induced by methyl vinyl ketone and is concomitant with the polymerisation reaction. Somewhat similar observations have been made with *tert.*-butylmagnesium halides which yield appreciable proportions of hexamethylethane when reacting with carbonyl compounds, although none of the hydrocarbon is obtained by the interaction of the halides and Grignard reagents alone (Whitmore, Stehman, and Herndon, *J. Amer. Chem. Soc.*, 1933, **55**, 3807; Shine, *J.*, 1951, 11). Evidence has been adduced that the coupling does *not* involve a free-radical process, and although no certain conclusions can be drawn, it seems likely that the same applies in the present case, and that the coupling may arise as a side reaction of the polymerisation of the methyl vinyl ketone by the lithium alkenyl. Other instances of such polymerisation have been investigated in detail by Ziegler and his co-workers (cf. *Annalen*, 1929, **473**, 1; 1934, **511**, 13 *et seq.*).

The reactions of *iso*butenyl-lithium with methyl propyl ketone and with mesityl oxide afforded low yields of the carbinols (I) and (III), together with higher-boiling products, but no dimethylhexadiene was isolated. The low yields (10—15%) of the carbinols contrast with those obtained from the corresponding ethylenic aldehydes (cf. Part II, *loc. cit.*, and below). The carbinol (III), a low-melting solid, has previously been prepared by Fellenberg (*Ber.*, 1904, **37**, 3578) in 2·5% yield from phorone and methylmagnesium iodide; a greatly improved yield (60%) has now been obtained by employing methylmagnesium bromide.

$$CHMe{:}CH{\cdot}COMe \xrightarrow{CMe_2{:}CHLi} \underset{(I)}{CHMe{:}CH{\cdot}CMe(OH){\cdot}CH{:}CMe_2} \xrightarrow{H^+} \underset{(II)}{CHMe{:}CH{\cdot}CMe{:}CH{\cdot}CMe_2{\cdot}OH}$$

Both the carbinols (I) and (III) readily undergo the usual oxotropic rearrangement in the presence of dilute acids. The rearrangement of (I) was not examined in detail, but by analogy with earlier work on unsymmetrical systems (Part II, *loc. cit.*), the initial product is expected to be the tertiary isomer (II). The rearrangement of the symmetrical carbinol (III) can only give one product (IV). The constitution of (IV) was confirmed by catalytic hydrogenation to 2 : 4 : 6-trimethylheptan-2-ol, characterised as the 3 : 5-dinitrobenzoate, and by an alternative synthesis from methylmagnesium bromide and methyl 3 : 5-dimethylhexa-2 : 4-dienoate (V), obtained by the Reformatski reaction of mesityl oxide and methyl bromoacetate. The carbinol (IV) exhibits anomalous ultra-violet light absorption; the maximum is at somewhat shorter wave-length (2290 Å) than expected for a trialkylated diene and the extinction coefficient (ε, 8000) is less than half the usual value. Similar anomalies are shown by 1 : 1 : 3-trimethylbutadiene (Lunt and Sondheimer, *J.*, 1950, 2957) and by the ester (V); they undoubtedly arise from steric hindrance to a coplanar all-*trans*-configuration of the conjugated systems and will be discussed in more detail in another series (cf. *J.*, 1949, 1890; Part I, *loc. cit.*).

$$\begin{array}{ccccc} CMe_2{:}CH{\cdot}COMe & \xrightarrow{CMe_2{:}CHLi} & \underset{(III)}{CMe_2{:}CH{\cdot}CMe(OH){\cdot}CH{:}CMe_2} & \xleftarrow{MeMgBr} & CMe_2{:}CH{\cdot}CO{\cdot}CH{:}CMe_2 \\ & & \downarrow H^+ & & \\ & & \underset{(IV)}{CMe_2{:}CH{\cdot}CMe{:}CH{\cdot}CMe_2{\cdot}OH} & \xleftarrow{MeMgBr} & \underset{(V)}{CMe_2{:}CH{\cdot}CMe{:}CH{\cdot}CO_2Me} \end{array}$$

In contrast to its reaction with the ethylenic ketones, the addition of *iso*butenyl-lithium to β-methylcrotonaldehyde gives a 50% yield of the expected di*iso*butenylcarbinol (VI). This is extremely sensitive to acids and probably represents the most mobile oxotropic system yet described. Although it contains one methyl substituent less than the homologue (III), it rearranges even more readily and is completely isomerised to (VII) by 0·001N-hydrochloric acid at room temperature in a few minutes. The great sensitivity of di*iso*butenylcarbinol to traces of acidic impurities and the ease of dehydration of its isomer to the triene (VIII) render the isolation of both carbinols difficult except under very carefully controlled conditions. An attempt to prepare di*iso*butenyl carbinol by the reduction of phorone with lithium aluminium hydride yielded mainly the triene (VIII).

$$CMe_2{:}CH{\cdot}CHO \xrightarrow{CMe_2{:}CHLi} CMe_2{:}CH{\cdot}CH(OH){\cdot}CH{:}CMe_2 \ (VI) \xrightarrow{H^+}$$

$$CMe_2{:}CH{\cdot}CH{:}CH{\cdot}CMe_2{\cdot}OH \ (VII) \xrightarrow{-H_2O} CMe_2{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH_2 \ (VIII)$$

Experimental

(All reactions were carried out under purified nitrogen. M. p.s were taken on a Kofler block and are corrected.)

iso*But-1-enyl-lithium*.—The preparation of *iso*butenyl chloride was adapted from Kirrman (*Bull. Soc. chim.*, 1948, **15**, 163). *iso*Butaldehyde (170 g.) was added to phosphorus pentachloride (500 g.) at 0°. After the vigorous initial reaction, the mixture was kept for 2 hours with occasional shaking and then added dropwise to ice-water (3 l.). The product was extracted with ether (1 l.), and the ethereal solution was dried ($CaCl_2$) and fractionated, giving 1 : 1-dichloro-3-methylpropane (135 g.), b. p. 107—108°. The latter was added in small portions to potassium hydroxide (65 g.) in ethylene glycol (300 ml.). The mixture was kept at 120° for 6 hours and then slowly distilled, giving *iso*butenyl chloride (50 g.) which after refractionation from a trace of sodium had b. p. 63°/740 mm., n_D^{20} 1·4192. A sample kindly given to us by Dr. S. H. Harper had b. p. 67°/750 mm., n_D^{19} 1·4212. Kirrman (*loc. cit.*) gives b. p. 67—69°, n_D^{20} 1·422; Frank and Blackham (*J. Amer. Chem. Soc.*, 1950, **72**, 3283) give b. p. 76°/740 mm., n_D^{20} 1·4224.

For the formation of *iso*butenyl-lithium, the chloride (46 g., 0·5 mole) is slowly added to a stirred suspension of finely-cut lithium (6·9 g., 1 mole) in sodium-dried ether (1 l.) (cf. Part I, *J.*, 1950, 2000). Reaction sets in after approx. ½ hour and is completed by gentle refluxing overnight. Less than 0·5 g. of unchanged metal then remains and is conveniently removed by means of a wire-gauze spoon.

Reaction with Methyl Vinyl Ketone.—Anhydrous methyl vinyl ketone (40 g.) in ether (50 ml.) was added slowly to a stirred ethereal solution of *iso*butenyl-lithium (from Li, 6·9 g.) at 0°. After 2 hours, saturated aqueous ammonium chloride solution (500 ml.) was added. Insoluble polymeric material (20 g.) was filtered off and the ethereal layer was separated, dried, and fractionated, giving 2 : 5-dimethylhexa-2 : 4-diene (9 g., 33%), b. p. 60—65°/135 mm., n_D^{22} 1·4752, $\lambda_{max.}$ 2420 Å, ε 21 500 (in EtOH), which solidified on cooling to 0° and formed crystals, m. p. 10° (Braude and Timmons, Part I, *loc. cit.*, give m. p. 11°, n_D^{18} 1·4780, and $\lambda_{max.}$ 2410 Å, ε 22 500).

Reaction with Methyl Propenyl Ketone.—Fractionation of a commercial sample of the ketone gave material boiling over the range 122—124°/770 mm., but of constant refractive index (n_D^{20} 1·4340) which contained about 15% of mesityl oxide as indicated by the intensity of an absorption band at 1660 cm.$^{-1}$ in the infra-red spectrum, kindly determined by Dr. E. S. Waight. The ketone (42 g.) in ether (50 ml.) was added dropwise to a stirred ethereal solution of *iso*butenyl-lithium (from Li, 6·9 g.) at 0°. Stirring was continued for 2 hours, excess of aqueous ammonium chloride was then added, and the ethereal layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated, giving the following products: (i) unchanged methyl propenyl ketone (8 g.), b. p. 65°/130 mm., identified as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 158°; (ii) unchanged mesityl oxide (6·5 g., 13%), b. p. 70°/130 mm., identified as the 2 : 4-dinitrophenylhydrazone which was chromatographed (alumina–benzene) and had m. p. and mixed m. p. 202—203° (Found: C, 51·5; H, 5·2; N, 19·7. Calc. for $C_{12}H_{14}O_4N_4$: C, 51·9; H, 5·1; N, 20·1%); (iii) iso*butenylmethylpropenylcarbinol* (2 : 4-*dimethylhepta*-2 : 5-*dien*-4-*ol*)

(10·4 g., 15%), which after refractionation had b. p. 77—79°/17 mm., n_D^{22} 1·4667 (Found : C, 77·3; H, 11·3. $C_9H_{16}O$ requires C, 77·1; H, 11·5%), and exhibited no light absorption with $\varepsilon > 1000$ in the 2200—4000-Å range in ethanol containing 0·1% of sodium ethoxide; (iv) a higher-boiling product (13 g.), b. p. 140°/0·5 mm., n_D^{23} 1·4922 (Found : C, 73·3; H, 9·1%), which exhibited no light absorption with $E_{1\,cm.}^{1\%} > 100$ in the 2200—4000-Å range. It did not form a 2 : 4-dinitrophenylhydrazone and was not further investigated.

On treatment with 0·002M-hydrochloric acid in 60% acetone for 1 hour at room temperature, the above dienol was converted into a conjugated isomer, formulated as **2 : 4-*dimethylhepta*-3 : 5-*dien*-2-*ol***, b. p. 95°/16 mm., n_D^{22} 1·4802 (Found : C, 77·8; H, 11·1. $C_9H_{14}O$ requires C, 77·1; H, 11·5%). Light absorption in ethanol : maximum, 2280 Å (ε 13 000), inflexion, 2350 Å (ε 12 000).

Reaction with Mesityl Oxide.—Mesityl oxide (25 g.) in ether (50 ml.) was added during 1 hour to an ethereal solution of *iso*butenyl-lithium (from Li, 3 g.) at 0°. Stirring was continued for 1 hour and then excess of aqueous ammonium chloride was added. The products were isolated as above and fractionated through a 12" Fenske column, giving (i) unchanged mesityl oxide (4 g.), b. p. 65°/110 mm., identified as the 2 : 4-dinitrophenylhydrazone, m. p. 203°; (ii) di*iso*butenylmethylcarbinol (2 : 4 : 6-trimethylhepta-2 : 5-dien-4-ol) (2 g., 8%), b. p. 36°/0·2 mm., which solidified on being kept and after recrystallisation from pentane had m. p. 56°, undepressed on admixture with the authentic sample described below, (iii) a higher-boiling product (14·4 g.), b. p. 81°/0·2 mm., n_D^{19} 1·4722, which solidified on being kept and crystallised from pentane in needles, m. p. 73—74°, and showed no light absorption with $E_{1\,cm.}^{1\%} > 100$ in the 2200—4000-Å range (Found : C, 74·0; H, 10·3%; *M*, in camphor, 196). It did not form a 2 : 4-dinitrophenylhydrazone and was not further investigated.

2 : 4 : 6-*Trimethylhepta*-2 : 5-*dien*-4-*ol* (III).—Phorone (30 g., m. p. 28°; prepared by the method of Cologne and Dumont, *Bull. Soc. chim.*, 1947, **14**, 38) in ether (40 ml.) was added dropwise to a stirred solution of methylmagnesium bromide (from Mg, 6 g.) in ether (250 ml.) at 0°. Stirring was continued for 2 hours and saturated aqueous ammonium chloride (500 g.) was then added. The ethereal layer was separated, the aqueous layer was extracted with ether (3 × 150 ml.), and the united ether solutions were dried (Na_2SO_4–K_2CO_3) and fractionated, giving the carbinol (20 g., 60%), b. p. 41°/0·2 mm., n_D^{21} 1·4638, which crystallised from pentane in needles, m. p. 56° (Found : C, 77·9; H, 11·9. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%). Fellenberg (*Ber.*, 1904, **37**, 3578) gives b. p. 43—46°/0·25 mm., m. p. 57·5°, and states that no satisfactory analytical data could be obtained owing to rapid aerial oxidation. We find that the carbinol is reasonably stable when pure. It reacted vigorously with methylmagnesium iodide in ether and exhibited no light absorption with $\varepsilon > 1000$ in the range 2200—4000-Å in ethanol containing 0·1% of sodium ethoxide.

2 : 4 : 6-*Trimethylhepta*-3 : 5-*dien*-2-*ol* (IV) and **2 : 4 : 6-*Trimethylheptan*-2-*ol*.**—(*a*) 2 : 4 : 6-Trimethylhepta-2 : 5-dien-4-ol (4·0 g.) was dissolved in 0·001M-solution of hydrochloric acid in 60% aqueous acetone (100 ml.) at room temperature. After 10 minutes, potassium carbonate (200 mg.) was added and most of the acetone removed under reduced pressure (100 mm.). The remaining solution was extracted with ether, and the ethereal extract was dried (Na_2SO_4–K_2CO_3) and fractionated, giving **2 : 4 : 6-*trimethylhepta*-3 : 5-*dien*-2-*ol*** (3·4 g.), b. p. 41°/0·2 mm., n_D^{21} 1·4715 (Found : C, 77·8; H, 12·0. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%). Light absorption in ethanol : maximum, 2280 Å (ε 8000), inflexion, 2360 Å (ε 7400).

The above dienol (3 g.) in methanol (30 ml.) was shaken with platinic oxide (10 mg.) in hydrogen until 880 ml. of hydrogen at 20°/765 mm. (Calc., 930 ml.) had been absorbed. Isolation of the product gave **2 : 4 : 6-*trimethylheptan*-2-*ol*** (2·6 g.), b. p. 85—88°/25 mm., n_D^{23} 1·4352 (Found : C, 75·7; H, 13·9. $C_{10}H_{22}O$ requires C, 75·9; H, 14·0%). The **3 : 5-*dinitrobenzoate*** crystallised from aqueous methanol in needles, m. p. 81—83° (Found : N, 8·1. $C_{17}H_{24}O_6N_2$ requires N, 7·95%).

(*b*) A mixture of mesityl oxide (66 g.) and methyl bromoacetate (102 g.) was added to zinc turnings (44 g.) in boiling benzene (300 ml.) during ½ hour (cf. Rupe and Lotz, *Ber.*, 1903, **36**, 15; Auwers and Eisenlohr, *J. pr. Chem.*, 1911, **84**, 93). When the vigorous reaction had subsided, the mixture was refluxed for a further 3 hours and then allowed to cool. Sulphuric acid (50 ml.) in water (300 ml.) was added and, after ½ hour, the benzene layer was separated. The aqueous layer was extracted with ether (3 × 100 ml.) and the combined extracts were fractionated, giving ***methyl* 3 : 5-*dimethylhexa*-2 : 4-*dienoate*** (50 g., 48%), b. p. 74°/0·5 mm., n_D^{23} 1·4761, $\lambda_{max.}$ 2700 and 2800 Å (ε 6500 and 6300, respectively) in ethanol (Found : C, 69·6; H, 9·1. $C_9H_{14}O_2$ requires C, 70·1; H, 9·2%). The ester failed to give an adduct on treatment with maleic anhydride in benzene.

The ester (13 g.) in ether (25 ml.) was added dropwise to a stirred solution of methylmagnesium bromide (from Mg, 5 g.) in ether (150 ml.) at 0°. Next day, excess of aqueous ammonium chloride was added and the products were worked up as above, giving 2 : 4 : 6-trimethylhepta-3 : 5-dien-2-ol (11·5 g., 82%), b. p. 40°/0·2 mm., n_D^{21} 1·4680, $\lambda_{max.}$ 2290 Å (ε 8000), $\lambda_{infl.}$ 2360 Å (ε 7400) in ethanol.

The dienol (2·5 g.) in methanol (30 ml.) in the presence of platinic oxide (10 mg.) absorbed 740 ml. of hydrogen at 760 mm./20° (Calc., 780 ml.), giving 2 : 4 : 6-trimethylheptan-2-ol (2 g.), b. p. 82°/23 mm., n_D^{22} 1·4345. It formed a 3 : 5-dinitrobenzoate, m. p. 79—83°, undepressed on admixture with the sample described above.

2 : 6-*Dimethylhepta*-2 : 5-*dien*-4-*ol* (VI).—β-Methylcrotonaldehyde (6·5 g.), b. p. 79—81°/116 mm. (prepared by the method of Young and Linden, *J. Amer. Chem. Soc.*, 1947, **69**, 2912), in ether (20 ml.) was added dropwise to an ethereal solution of *iso*butenyl-lithium (from Li, 2·3 g.) at 0°. After 2 hours, excess of aqueous ammonium chloride was added and the products were worked up as above, giving 2 : 6-*dimethylhepta*-2 : 5-*dien*-4-*ol* (4·6 g., 48%), b. p. 43—44°/0·4 mm., n_D^{23} 1·4833 (Found : C, 76·8, H, 11·2. $C_9H_{16}O$ requires C, 77·1; H, 11·5%). A solution of the dienol in ethanol containing 0·1% of sodium ethoxide showed no light absorption with ε >1000 in the range 2200—4000 Å. The dienol is very unstable in air and repetitions of this preparation under apparently identical conditions often gave partly rearranged and dehydrated material.

2 : 6-*Dimethylhepta*-3 : 5-*dien*-2-*ol* (VII) *and* 2 : 6-*Dimethylhepta*-1 : 3 : 5-*triene* (VIII).—The above dienol (3 g.) was dissolved in an 0·001M-solution of hydrochloric acid in 60% aqueous acetone (50 ml.) at room temperature. After 10 minutes, potassium carbonate (100 mg.) was added and the product worked up as above, giving 2 : 6-*dimethylhepta*-3 : 5-*dien*-2-*ol* (2·1 g.), b. p. 42°/0·05 mm., n_D^{16} 1·4983 (Found : C, 77·2; H, 11·2. $C_9H_{16}O$ requires C, 77·1; H, 11·5%). Light absorption in ethanol : maximum, 2370 Å; ε 20 000.

On being kept, or on treatment with more concentrated mineral acid, the carbinol slowly underwent dehydration, and distillation from a trace of potassium hydrogen sulphate afforded 2 : 6-*dimethylhepta*-1 : 3 : 5-*triene*, b. p. 54°/15 mm., 32°/0·1 mm., n_D^{21} 1·5130—1·5190, which was not obtained completely pure (Found : C, 86·2; H, 11·5. C_9H_{14} requires C, 88·4; H, 11·5%). Light absorption in ethanol : maxima, 2610, 2700, and 2880 Å; ε 22 000, 32 000, and 24 000, respectively. The triene (5 g.) was also the main product obtained by the action of lithium aluminium hydride (2 g.) on phorone (9 g.) in ether at −10°.

Reaction of iso*Butenyl Phenyl Ketone with Methyl-lithium.*—The ketone (15 g.; prepared by Darzens's method, *Compt. rend.*, 1929, **189**, 767) in ether (50 ml.) was added to a solution of methyl-lithium (from Li, 1·4 g.; methyl bromide, 9 g.) in ether (300 ml.). After 2 hours, excess of aqueous ammonium chloride was added. The products were isolated in the usual way and fractionated from a trace of potassium carbonate, giving 4-methyl-2-phenylpent-3-en-2-ol (13 g., 80%), b. p. 64°/0·3 mm., n_D^{21} 1·5286 (Braude and Coles, Part III, *loc. cit.*, give n_D^{20} 1·5289). The first fractions, on treatment with Brady's reagent, gave a small quantity (30 mg.) of a red 2 : 4-*dinitrophenylhydrazone* which crystallised from dioxan in plates, m. p. 277—278°, $\lambda_{max.}$ 3850 Å ($E_{1\,cm.}^{1\%}$ 900, in chloroform) (Found : N, 15·9. $C_{18}H_{20}O_4N_4$ requires N, 15·7%). The analytical data correspond to the derivative of *neo*pentyl phenyl ketone.

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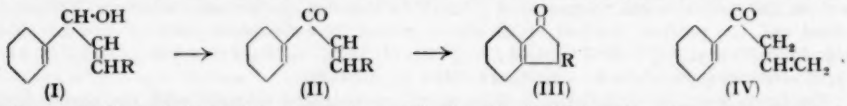
261. *Syntheses of Polycyclic Systems. Part III.* Some Hydroindanones and Hydrofluorenones. The Mechanism of the Nazarov Cyclisation Reaction.*

By E. A. Braude and J. A. Coles.

Oxidation of 1-*cyclo*hex-1′-enylalken-1-ols (I) (*J.*, 1950, 2014) with manganese dioxide affords the alkenyl *cyclo*hexenyl ketones (II) which undergo cyclisation with phosphoric acid to tetrahydro-indanones (III). Di*cyclo*hexenyl ketone (V) under similar conditions gives decahydrofluorenone (VI) (probably *cis*), which is catalytically hydrogenated to *syn*-perhydrofluorenone (probably *cis-cis*). The mechanism of the cyclisation reaction is discussed.

A versatile route to hydroaromatic structures containing five-membered rings, which has been explored within recent years by Nazarov and his co-workers (cf. *Bull. Acad. Sci. U.R.S.S., Cl. Sci. chim.*, 1946, 633; 1947, 205; *J. Gen. Chem. Russia*, 1950, **20**, 2009), consists in the cyclisation of substituted allyl vinyl ketones in the presence of moderately strong acids. For instance, allyl *cyclo*hexenyl ketone (IV) is converted into 4 : 5 : 6 : 7-tetrahydro-3-methylindanone (III; R = Me) on treatment with phosphoric and formic acids. Theoretical considerations, which are discussed below, suggested that the corresponding substituted divinyl ketones (*e.g.*, II) should similarly give the same products. Such ketones have recently become readily accessible by direct alkenylation with lithium alkenyls (Braude and Coles, *J.*, 1950, 2012, 2014), and, in the present paper, the cyclisation of three of them is described.



*cyclo*Hexenyl vinyl and propenyl ketones (II; R = H and Me) were conveniently prepared by manganese dioxide oxidation (cf. Weedon and Woods, *J.*, 1951, 2687; Braude and Forbes, *ibid.*, p. 1755) of the corresponding carbinols (I; R = H and Me), previously obtained by the reaction of *cyclo*hexenyl-lithium with acraldehyde and crotonaldehyde respectively (Braude and Coles, *loc. cit.*). The ketones exhibited the expected ultra-violet light absorption properties (see Table) and were characterised by their 2 : 4-dinitrophenylhydrazones. A mixture of phosphoric and formic acids, under conditions identical with those employed by Nazarov and Pinkina (*loc. cit.*, 1947), converted them, in 50—70% yields, into the tetrahydroindanones (III; R = H and Me).

The position of the ethylenic bond in the tetrahydroindanones follows from their ultra-violet light absorption characteristics (see Table): the presence of maxima at 2370 and 3000 Å shows that the double bond is conjugated with the carbonyl group; the fact that the location of the high-intensity band is entirely unaffected by the introduction of a 3-methyl substituent excludes the 2 : 3-position (as in VIII, see below), and the fact that $\lambda_{max.}$ lies below 2400 Å excludes the 7 : 8-position (cf. Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 76); the 8 : 9-position is thus the only possible one. As in the case of other *cyclo*pentenones (cf. Gillam and West, *J.*, 1942, 486; Frank, Armstrong, Kwiatek, and Price, *J. Amer. Chem. Soc.*, 1948, **70**, 1379; Crombie and Harper, *J.*, in the press) the high-intensity bands of the indanones (III) lie at considerably *shorter* wave-lengths than those of the corresponding open-chain analogues; on the other hand, the positions of the characteristic maxima of the 2 : 4-dinitrophenylhydrazones are quite normal (Braude and Jones, *J.*, 1945, 498).

4 : 5 : 6 : 7-Tetrahydroindanone has previously been synthesised in low yield by cyclisation of β-*cyclo*hexenylpropionic acid (Nenitzescu and Przemetzky, *Ber.*, 1941, **74**, 676; Mathieson, *J.*, 1951, 177), as well as of the corresponding succinic half-ester (Johnson, Davis, Hunt, and Stork, *J. Amer. Chem. Soc.*, 1948, **70**, 3021). Since the completion of the present work, Nazarov and Pinkina's synthesis of 4 : 5 : 6 : 7-tetrahydro-3-methylindanone

* Part II, *J.*, 1951, 3117.

has been re-examined by Hamlet, Henbest, and Jones (*J.*, 1951, 2653) who showed that extensive cyclisation of (IV) already takes place during its formation by the hydration of 4-*cyclo*hexenylbut-1-en-3-yne in the presence of mercuric oxide and sulphuric acid. These authors also determined the light-absorption properties of the ketones (III) with results similar to those obtained here. The identity of the tetrahydromethylindanones obtained by the two routes was confirmed by the mixed melting points of the 2 : 4-dinitrophenylhydrazones; we are indebted to Professor E. R. H. Jones and Dr. H. B. Henbest for kindly providing a sample.

Light absorption data.

	Dialkenyl ketone *		2 : 4-Dinitrophenylhydrazone †	
	$\lambda_{max.}$, Å	ε	$\lambda_{max.}$, Å	ε
(II; R = H)	2510	7 500	3850	21 500
	3300	30		
(II; R = Me)	2570	14 600	3860	29 400
	3280	80		
(V)	2420	16 500	3880	30 600
	3190	90		
	*cyclo*Pentenone *		2 : 4-Dinitrophenylhydrazone †	
(III; R=H)	2370	12 500	3900	27 500
	3000	50		
(III; R = Me)	2370	12 500	3920	26 400
	3020	60		
(VI)	2400	12 500	3980	25 500
	3040	70		

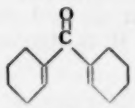
* In ethanol solution (the weak long-wave-length bands appear as inflections).
† In chloroform solution (main band only).

As a further example, di*cyclo*hexenyl ketone (V), obtained by the reaction of *cyclo*hexenyl-lithium with carbon dioxide (Braude and Coles, *loc. cit.*), has been cyclised to the decahydrofluorenone (VI), a low-melting solid. Catalytic dehydrogenation of the latter in the presence of palladised charcoal at 300° afforded fluorene but no trace of fluorenone; reduction of keto-groups accompanying dehydrogenation under similar conditions has been observed in a number of other cases (cf. Linstead and Michaelis, *J.*, 1940, 1134; Newman and Zahm, *J. Amer. Chem. Soc.*, 1943, **65**, 1097). Catalytic hydrogenation of (VI) in the presence of platinic oxide gave a liquid perhydrofluorenone. Its crystalline oxime was identical (mixed melting point) with that of the *syn*-perhydrofluorenone obtained by Davis, Doering, Levine, and Linstead (*J.*, 1950, 1423) by the pyrolysis of *syn*-perhydrodiphenic acids; we are indebted to Professor R. P. Linstead for kindly providing a sample.

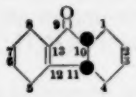
Davis *et al.* (*loc. cit.*) were not able to decide the steric orientation of the 10- and the 13-hydrogen atom in their *syn*-perhydrofluorenone, but a tentative assignment can now be made. Catalytic hydrogenation of the 12 : 13-ethylenic bond in the decahydrofluorenone (VI) most probably involves *cis*-addition in the normal manner,* so that the 12 : 13-ring-junction in the *syn*-perhydrofluorenone will be *cis*. Furthermore, the fact that only *one* perhydrofluorenone appears to be formed indicates that the 10 : 11-ring junction in the antecedent decahydrofluorenone (the homogeneity of which is not in doubt) and, therefore, in the perhydrofluorenone, is also *cis*, as shown. *cis*-Decahydrofluorenone (VI) will be preferentially adsorbed owing to catalyst hindrance (Linstead, Doering, Davis, Levine, and Whetstone, *J. Amer. Chem. Soc.*, 1942, **64**, 1985) in such a way that the two unsaturated rings are nearly flat, with the 10 : 11-hydrogen atoms directed towards, and the saturated ring directed away from, the catalyst surface; addition of hydrogen to the 12 : 13-bond will thus take place on the same side as the 10 : 11-hydrogen atoms, giving *cis-syn-cis*-perhydrofluorenone (VII). If, on the other hand, the ring junction in the decahydrofluorenone were *trans*, very little steric preference would be expected for either of the two possible modes of accommodation on the catalyst and a mixture of *syn*- and *anti*-perhydrofluorenones should result. It is interesting that the probable production of a *cis*-ring-junction in the cyclisation of (V) to (VI) is paralleled by the formation of *cis*-decalin derivatives in the somewhat related cyclisation of diolefins (Hibbit, Linstead, and Millidge, *J.*, 1936, 470, 476; Elliott and Linstead, *J.*, 1938, 662).

* *trans*-Addition in the hydrogenation of $\alpha\beta$-ethylenic ketones has been observed under special conditions (cf. Weidlich, *Chemie*, 1945, **58**, 30).

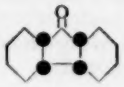
The present results provide some evidence concerning the mechanism of the cyclisation of diethylenic ketones. This reaction closely resembles the acid-catalysed cyclisation of diethylenic hydrocarbons (cf. Linstead *et al.*, *loc. cit.*, 1938; Stevens and Spalding, *J. Amer. Chem. Soc.*, 1949, **71**, 1687, and earlier references there cited), of benzenoid hydrocarbons



(V)

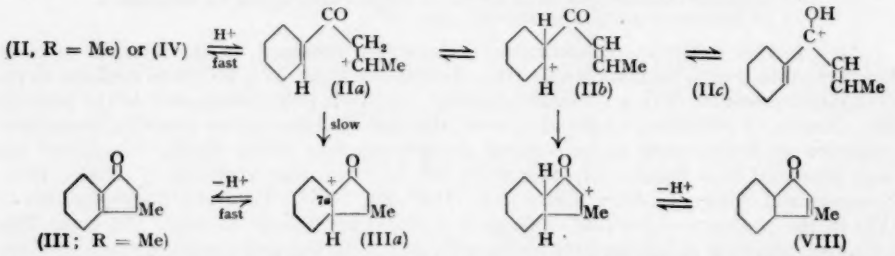


(VI)



(VII)

containing an ethylenic side chain (cf. Bogert *et al.*, *J. Amer. Chem. Soc.*, 1934, **56**, 185; 1935, **57**, 151; *J. Org. Chem.*, 1936, **1**, 288; 1941, **6**, 105, and references there cited), and, more particularly, of ψ-ionone to α- and β-ionone (cf. Hibbert and Cannon, *J. Amer. Chem. Soc.*, 1924, **46**, 126), but it appears to take place somewhat less readily. There can be little doubt that the prime function of the acid medium in all these reactions is that of proton-donor, and that the ethylenic compound, acting as a weak base, is partly converted into a carbonium ion by reversible addition of one or more protons. The facts that the ketones (II) and (IV) give the same product and react with comparable rates are consistent with the formulation of the intermediate as (II*a*); the subsequent steps of the reaction consist of the formation of the new carbon–carbon link accompanied by the transference of the positive charge to $C_{(7a)}$ and the reversible loss of a proton from the new carbonium ion (III*a*). In the ethylenic ketones, the carbonyl group will compete as a basic centre



with the ethylenic groups and deactivate the latter, but although the ion (II*c*) in which the proton is attached to the carbonyl group may predominate, (II*a*) will exist in equilibrium with it, as well as with the corresponding ion (II*b*) in which the proton is attached to the *cyclo*hexenyl group. The deactivating effect of the keto-group is clearly shown by the fact that the Nazarov cyclisation of dialkenyl ketones occurs less readily than the related reactions mentioned above, and also by the direction of cyclisation of ψ-ionone, which leads to the disappearance of the *unconjugated* double bond. Cyclisation of (II*b*) would lead to the ketone (VIII); since none of the latter is detected, the rate of cyclisation of (II*a*) must be rather faster than that of (II*b*), or, as appears more likely, the equilibrium proportion of (II*a*) must be considerably higher than that of (II*b*). This leads to the conclusion that the basicity of the propenyl group must be greater than that of the *cyclo*hexenyl group and, since (III; R = H) appears to be the sole product from the lower homologue, the same applies to the vinyl group.

Experimental

(M. p.s marked K were determined on a Kofler block and are corrected. For light absorption data, see Table.)

cyclo*Hex*-1-*enyl Vinyl Ketone*.—1-*cyclo*Hex-1′-enylprop-2-en-1-ol (10 g.; Braude and Coles, *J.*, 1950, 2014), light petroleum (b. p. 40—60°; 1 l.; distilled from sodium) and manganese dioxide (100 g.; vacuum-dried) were shaken together for 3 days in a brown, glass-stoppered bottle in an atmosphere of nitrogen. After filtration, the solvent was distilled off through an 8″ Fenske column, and the product was fractionated, giving the *ketone* (9 g.), b. p. 47—48°/0·1 mm., n_D^{22} 1·5100 (Found: C, 79·4; H, 9·3. $C_9H_{12}O$ requires C, 79·4; H, 8·9%). The 2 : 4-*dinitrophenylhydrazone*, after chromatography (alumina–benzene), crystallised from ethyl acetate–

ethanol in orange plates, m. p. 210—211° (Found: C, 56·8; H, 5·1; N, 17·5. $C_{15}H_{16}O_4N_4$ requires C, 56·95; H, 5·1; N, 17·7%).

4 : 5 : 6 : 7-*Tetrahydroindanone*.—A mixture of the above ketone (5 g.), phosphoric acid (2 g.), and formic acid (98%; 6 g.) was kept at 80—90° for 4 hours under nitrogen. After cooling, the mixture was carefully added to water (200 ml.), and the resulting solution was extracted with ether. The ethereal extract was washed with 10% aqueous sodium carbonate and water, dried (Na_2SO_4), and distilled, giving the indanone (2·5 g.), b. p. 126—128°/14 mm., n_D^{23} 1·5189 (Found: C, 78·8; H, 9·05. Calc. for $C_9H_{12}O$: C, 79·4; H, 8·9%) (Nenitzescu and Przemetzky, *Ber.*, 1941, **74**, 685, give b. p. 124—125°/17 mm., n_D^{20} 1·5235). The 2 : 4-dinitrophenylhydrazone crystallised from benzene in orange plates, m. p. 235° (K) (Found: C, 56·6; H, 5·5; N, 17·6. Calc. for $C_{15}H_{16}O_4N_4$: C, 56·95; H, 5·1; N, 17·7%) (Johnson *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 3022, and Mathieson, *J.*, 1951, 177, give m. p. 238°).

cyclo*Hex*-1-*enyl Propenyl Ketone*.—1-*cyclo*Hexen-1′-enylbut-2-en-1-ol (15 g.; Braude and Coles, *loc. cit.*), light petroleum (b. p. 40—60°; 1 l.) and manganese dioxide (100 g.) gave, as above, the *ketone* (12 g.), b. p. 64—65°/0·3 mm., n_D^{19} 1·5164 (Found: C, 80·4; H, 9·7. $C_{10}H_{14}O$ requires C, 80·0; H, 9·4%). The 2 : 4-*dinitrophenylhydrazone* was chromatographed (alumina–benzene) and crystallised from ethyl acetate in red prisms, m. p. 152° (Found: C, 58·4; H, 5·6; N, 16·85. $C_{16}H_{18}O_4N_4$ requires C, 58·1; H, 5·5; N, 16·95%).

Attempted oxidation of the carbinol with acetone and aluminium *tert.*-butoxide in benzene failed, mainly unchanged starting materials being obtained after 30 hours' refluxing.

4 : 5 : 6 : 7-*Tetrahydro-3-methyl-indanone*.—A mixture of the foregoing propenyl ketone (6 g.), phosphoric acid (2·5 g.), and formic acid (98%; 7 g.) was kept at 90° for 7 hours under nitrogen. The products were worked up as above, giving the indanone (4 g.) as a colourless liquid, b. p. 114°/15 mm., n_D^{19} 1·5106 (Nazarov and Pinkina, *Bull. Acad. Sci. U.R.S.S., Cl. Sci. Chim.*, 1946, 633, give b. p. 104—106°/8 mm., n_D^{20} 1·5124). It formed a semicarbazone which separated from aqueous methanol in prisms, m. p. 214—217° (with decomp.) (Nazarov and Pinkina, *loc. cit.*, give m. p. 211°), and a 2 : 4-dinitrophenylhydrazone, which was chromatographed (alumina–benzene) and crystallised from chloroform in brilliant crimson prisms, m. p. 246—248° (K) (Found: N, 17·15. Calc. for $C_{16}H_{18}O_4N_4$: N, 17·0%). The m. p. was undepressed on admixture of the sample with the 2 : 4-dinitrophenylhydrazone since described by Hamlet, Henbest, and Jones (*J.*, 1951, 2658), who give m. p. 246°.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : (cis-?)10 : 11-*Decahydrofluorenone*.—A mixture of di*cyclo*hex-1-enyl ketone (3·5 g.; Braude and Coles, *loc. cit.*), phosphoric acid (*d* 1·7; 4 g.) and formic acid (98%; 5 g.) was kept at 90° for 10 hours under nitrogen. Working up as above gave an oily product which was then dissolved in pentane. Cooling in carbon dioxide–methanol caused crystallisation of the *decahydrofluorenone* (1 g.), m. p. 26° which was not raised on recrystallisation from pentane (Found: C, 81·9; H, 9·6. $C_{13}H_{18}O$ requires C, 82·0; H, 9·5%). It formed an *oxime*, which separated from light petroleum (b. p. 100—120°) in cream-coloured prisms, m. p. 133—134° (Found: N, 6·5. $C_{13}H_{19}ON$ requires N, 6·8%), and a 2 : 4-*dinitrophenylhydrazone* which was chromatographed (alumina–benzene–chloroform) and crystallised from ethanol–ethyl acetate in dark red needles, m. p. 168—169° (Found: N, 15·0. $C_{19}H_{22}O_4N_4$ requires N, 15·1%).

Dehydrogenation.—A mixture of decahydrofluorenone (1 g.) and 25% palladised charcoal (0·2 g.) was heated at 300° for 28 hours in a stream of nitrogen. The crude product gave no precipitate with Brady's reagent and on extraction with hot light petroleum (b. p. 60—80°) afforded fluorene (0·4 g.), m. p. 112—113°, undepressed on admixture of the specimen with an authentic sample. A similar experiment with 10% palladised charcoal at 200° for 2 hours yielded mainly unchanged starting material.

cis-syn-cis(?)-*Perhydrofluorenone*.—A solution of decahydrofluorenone (2·3 g.) in methanol (30 ml.) was shaken with platinic oxide (20 mg.) in hydrogen until 295 ml. (1 mol.) at 18°/750 mm. had been absorbed. The product was converted into the oxime which was crystallised from ethanol and had m. p. 171—173° (K), undepressed on admixture of the sample with the specimen of *syn*-perhydrofluorenone oxime (m. p. 169—171°), described by Davis, Doering, Levine, and Linstead (*J.*, 1950, 1423; cf. Hückel, *Annalen*, 1934, **508**, 10) who give m. p. 172—174°.

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262. *Reaction with Diazomethane and its Derivatives. Part III.* Action of Diazo-compounds on 2-Arylideneindane-1 : 3-diones and Methyleneanthrone.*

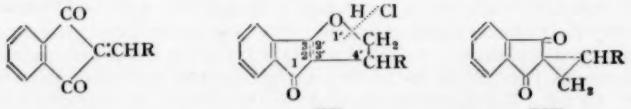
By AHMED MUSTAFA and MUSTAFA KAMAL HILMY.

2-Arylideneindane-1 : 3-diones (listed in the Table) react with ethereal diazomethane, in the presence or absence of methyl alcohol, to yield colourless or almost colourless substances, believed to be furanoindenones (II).

Methyleneanthrone (IV) reacts readily with diazomethane and its derivatives to form colourless crystals, believed to be *cyclo*propane derivatives (VI).

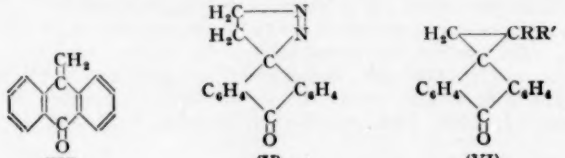
A NUMBER of the intensely coloured 2-arylideneindane-1 : 3-diones (I) (cf. the Table) react with ethereal diazomethane solution, in the presence or absence of methyl alcohol, giving the furanoindenones (II), which, except for the pale yellow nitro-compounds (II; R = C_6H_4·NO_2-*m* and -*p*) are colourless or substantially colourless. The reaction mechanism is believed to be similar to that proposed for *o*-hydroxyanils (Schönberg, Mustafa, and Hilmy, *J.*, 1947, 1045; Schönberg and Awad, *J.*, 1950, 72). It is improbable that the products are *cyclo*propane derivatives (III), since (II; R = C_6H_4·OMe-*p*) gives only a monoxime, does not give phthalic acid on treatment with alkali, and is thermostable at 160° for half an hour. There is of course a greater tendency to form a five-membered than a three-membered ring (strain theory).

With alcoholic hydrochloric acid (II; R = C_6H_4·OMe-*p*) gives a colourless product whence it is regenerated by pyridine; this product gives a ferric chloride colour and has one active hydrogen atom; it may be the furanoindanone 1′-oxonium salt or may be formed by addition of HCl across by 2 : 3-bond or by fission as indicated by the dotted line in (II). Hydrobromic acid in cold acetic acid leads to a similar product. Enols can be formed in each case.



(I) (II) (III)

Methyleneanthrone (IV) reacts readily with ethereal diazomethane in the presence of methyl alcohol, with strong evolution of gas, to give colourless product (VI; R = R′ = H), probably by way of (V). For a similar formation of a *cyclo*propane ring, compare the action of diazomethane on 9-methylenefluorene (Wieland and Probst, *Annalen*, 1937, **530**, 277). The product (VI; R = R′ = H) is crystalline, whereas 9-ethylideneanthrone is an unstable red oil, b. p. 245—247°/20 mm. (Julian, Cole, and Wood, *J. Amer. Chem. Soc.*, 1935, **57**, 2508); it reacts with one mol. of phenylmagnesium bromide to give the carbinol and on oxidation with chromic acid gives anthraquinone.



(IV) (V) (VI)

With diazoethane, (IV) similarly yields (VI; R = Me, R′ = H), and with diphenyldiazomethane (VI; R = R′ = Ph).

* The paper by Mustafa (*J.*, 1949, 256) is regarded as Part I and that by Mustafa and Hilmy (*J.*, 1951, 3254) as Part II.

Experimental

Action of Diazomethane on 2-Arylideneindane-1 : 3-diones (I). The dione (1 g.) in methyl alcohol (2 c.c.) was treated with ethereal diazomethane (from methylnitrosourea, 8 g.), and the mixture was left for 48 hours at 0°. The methyl alcohol and ether were evaporated off, and the residue was worked-up as follows (D denotes the deposit formed during the reaction, and R the residue obtained on evaporation of the reaction mixture) :

(*a*) R was dissolved in light petroleum (b. p. 60—80°), and the solution was allowed to evaporate slowly; the crystals which separated were recrystallised from the same solvent.

(*b*) R was washed with cold ethyl alcohol and crystallised from light petroleum (b. p. 80—100°).

(*c*) D was recrystallised from benzene–light petroleum (b. p. 30—50°); it was difficultly soluble in ethyl alcohol.

(*d*) D was washed repeatedly with ethyl alcohol; it was difficultly soluble in hot alcohol and light petroleum (b. p. 60—80°) and crystallised from benzene–light petroleum (b. p. 30—50°).

(*e*) R was treated with cold absolute ethyl alcohol, and crystallised from the same solvent.

(*f*) R was extracted with hot ethyl alcohol and the extract allowed to evaporate slowly; the crystals which separated were recrystallised from light petroleum (b. p. 60—80°).

(*g*) R was extracted several times with hot light petroleum (b. p. 60—80°) and the extract was allowed to evaporate slowly; the crystals which separated were recrystallised from the same solvent.

(*h*) R was crystallised from light petroleum (b. p. 80—100°).

(*i*) R was extracted several times with hot light petroleum (b. p. 80—100°); the crystals which separated were recrystallised from the same solvent.

The *products* are recorded in the Table. All gave a violet colour in concentrated sulphuric acid; this changed to green in (*a*) and (*b*).

4′-Substituted furano(3′ : 2′-2 : 3)indenones (II).

Ref.*	R	M. p.	Yield, %	Found, % C	H	N	Formula	Required, % C	H	N
a	Ph [1]	91—92°	40	82·1	4·8	—	$C_{17}H_{12}O_2$	82·2	4·8	—
b	*p*-MeO·C_6H_4 [2]	119	85	77·6	5·1	—	$C_{18}H_{14}O_3$ [4]	77·7	5·0	—
c	*m*-NO_2·C_6H_4 [2]	162—163	80	69·6	3·6	4·5	$C_{17}H_{11}O_4N$	69·6	3·7	4·8
d	*p*-NO_2·C_6H_4 [2]	168	82	69·6	3·8	4·4	$C_{17}H_{11}O_4N$ [5]	69·6	3·7	4·8
e	*p*-NMe_2·C_6H_4 [2]	102—103	50	78·2	5·9	4·8	$C_{19}H_{17}O_2N$	78·3	5·8	4·8
f	*p*-NEt_2·C_6H_4	75	30	78·7	6·7	4·5	$C_{21}H_{21}O_2N$	79·0	6·6	4·4
g	*p*-C_6H_4Cl [3]	92	40	72·0	3·9	—	$C_{17}H_{11}O_2Cl$ [6]	72·2	3·9	—
h	3 : 4-CH_2O_2·C_6H_3 [3]	110	70	74·0	4·0	—	$C_{18}H_{12}O_4$	74·0	4·1	—
i	2-Furyl [3]	126	50	75·3	4·3	—	$C_{15}H_{10}O_3$	75·6	4·2	—

* Cf. above.

[1] Wislicenus and Kotzle, *Annalen*, 1889, **252**, 73. [2] Petrow, Saper, and Sturgeon, *J.*, 1949, 2134. [3] Ionescu, *Bull. Soc. chim.*, 1930, **47**, 210. [4] Found : *M* (micro-Rast), 275. Reqd. : *M*, 278. [5] Found : *M* (micro-Rast), 290. Reqd. : *M*, 293. [6] Found : Cl, 12·5. Reqd. : Cl, 12·6%.

2-p-*Diethylaminobenzylideneindane-1 : 3-dione*.—Indane-1 : 3-dione (Teeters and Shriner, *J. Amer. Chem. Soc.*, 1933, **55**, 3026) (0·1 mole) and *p*-diethylaminobenzaldehyde (0·1 mole) were fused together at 130—140° (bath-temp.) for ½ hour. Water-vapour was vigorously evolved, the melt solidified on cooling, and the product was isolated by crystallisation from ethyl alcohol as violet red crystals (82%), m. p. 145° (Found : C, 78·5; H, 6·0; N, 4·4. $C_{20}H_{19}O_2N$ requires C, 78·7; H, 6·2; N, 4·6%).

Action of Hydroxylamine on (II; R = *p*-MeO·C_6H_4).—To a solution of the dione (0·4 g.) and hydroxylamine hydrochloride (0·55 g.) in ethyl alcohol (10 c.c.) was added a solution of potassium hydroxide (0·7 g.) in water (1 c.c.) (cf. Kohler, *J. Amer. Chem. Soc.*, 1919, **41**, 1254, 1261). The mixture was refluxed for 3 hours, poured into cold water, neutralised with dilute hydrochloric acid, and extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated, giving an oily residue. This was dissolved in hot ethyl alcohol, and on slow evaporation gave almost colourless crystals, m. p. 163—164°, from ethyl alcohol (Found : C, 73·4; H, 5·0; N, 4·4. $C_{18}H_{15}O_3N$ requires C, 73·7; H, 5·1; N, 4·8%).

Action of Hydrochloric Acid on (II; R = *p*-MeO·C_6H_4).—To a solution of *4′-p*-methoxyphenylfurano(3′ : 2′-2 : 3)indenone in ethyl alcohol (10 c.c.), hydrochloric acid (5 c.c.; *d* 1·18) was added. The mixture was refluxed for 2 hours and then poured into ice-cold water. The oil, that separated, was washed several times with small amounts of cold ethyl alcohol,

then becoming solid; it readily crystallised from benzene as colourless crystals, m. p. 110—111° (Found: C, 68·7; H, 4·7; Cl, 11·0; active H, 0·27. $C_{18}H_{15}O_3Cl$ requires C, 68·8; H, 4·8; Cl, 11·1; active H, 0·3%). The *substance* is easily soluble in light petroleum (b. p. 80—100°), hot ethyl alcohol, or hot benzene, and gave a violet colour in concentrated sulphuric acid. An alcoholic solution gave a reddish-violet colour when treated with alcoholic ferric chloride at 60°.

The product was boiled with pyridine for a few minutes and then poured into cold water and extracted with ether, and the extract washed with dilute cold hydrochloric acid, then with water, dried (Na_2SO_4), and evaporated. The resultant almost colourless crystals proved to be (II; R = *p*-MeO·C_6H_4) (m. p. and mixed m. p. and colour reaction with sulphuric acid).

Action of Hydrobromic Acid on (II; R = *p*-MeO·C_6H_4).—A saturated solution of dry hydrogen bromide in acetic acid (10 c.c.) was added to the dione (0·5 g.), and the reaction mixture was kept overnight at room temperature. It was then poured into ice-cold water, the brownish semi-solid *substance* that separated crystallised from benzene as pale yellow crystals, m. p. 177—178° [Found: C, 60·0; H, 4·0; Br, 22·1%; *M* (micro-Rast), 348. $C_{18}H_{15}O_3Br$ requires C, 60·1; H, 4·2; Br, 22·3%; *M*, 358·9]. This material is soluble in aqueous potassium hydroxide and gives a violet colour in concentrated sulphuric acid.

Reaction of Methyleneanthrone with Diazomethane.—Methyleneanthrone (1 g.) in methyl alcohol (2 c.c.) was treated with ethereal diazomethane solution as described for the 2-arylidene-1 : 3-indanediones. The crystals that separated recrystallised from benzene–light petroleum (b. p. 40—60°) in colourless crystals (VI), m. p. 152° (Found: C, 87·2; H, 5·4. $C_{16}H_{12}O$ requires C, 87·3; H, 5·5%) *Anthrone*-9-spirocyclo*propane* (VI; R = R′ = H) gives a yellow colour with a green fluorescene in concentrated sulphuric acid. Evaporation of the ethereal mother-liquor gave further quantity. The total yield is almost quantitative.

Action of phenylmagnesium bromide on (VI; R = R′ = H). To a Grignard solution of phenylmagnesium bromide [from magnesium (0·9 g.), bromobenzene (9 g.), and ether (50 c.c.)], dry benzene (30 c.c.) was added, and the mixture treated gradually with the foregoing spiran (powdered) (1 g.). The mixture was refluxed for 2 hours, set aside overnight, poured into aqueous ammonium chloride, and extracted with ether, and the extract dried (Na_2SO_4) and evaporated. Solid 10-*phenylanthranol*-9-spirocyclo*propane* that separated was washed twice with light petroleum (b. p. 40—60°) and crystallised from benzene as colourless crystals, m. p. 185—186° (Found: C, 88·4; H, 6·1; active H, 0·32. $C_{22}H_{18}O$ requires C, 88·6; H, 6·1; active H, 0·34%). This compound gives a dark brown colour with sulphuric acid and its benzene solution acquires a blue-violet fluorescene.

Oxidation. The anthrone-spiran (1 g.), in glacial acetic acid (20 c.c.), was treated on the boiling water-bath with chromic acid (2 g.) for 5 hours. The cooled mixture was poured into ice-cold water, and the separated solid was filtered off, washed thoroughly with water, and crystallised from xylene, in pale yellow crystals, m. p. 278°; it was identified as anthraquinone by its m. p. and mixed m. p. and colour reaction with zinc dust and aqueous ammonia.

Reaction of Methyleneanthrone with Diazoethane.—The oily residue after the excess of the ethereal diazoethane (Werner, *J.*, 1919, **115**, 1093) had been removed solidified on long storage and then was crystallised from ethyl alcohol, forming colourless crystals, m. p. 82° (Found: C, 87·1; H, 5·8. $C_{17}H_{14}O$ requires C, 87·2; H, 5·9%). 2′-*Methylanthrone*-9-spiro-1′-cyclo*propane* (VI; R = Me, R′ = H) is easily soluble in benzene or hot alcohol and gives a green colour with concentrated sulphuric acid.

Reaction of Methyleneanthrone with Diphenyldiazomethane.—The anthrone (1 g.) in benzene (20 c.c.) was treated with diphenyldiazomethane (Staudinger and Gaule, *Ber.*, 1916, **49**, 1897) [prepared from benzophenone hydrazone (1·2 g.) and yellow mercuric oxide (3 g.) suspended in benzene 50 c.c.]. The mixture was refluxed for 30 minutes. The deep red colour faded. The benzene was evaporated off, and the solid residue was washed with cold ether, followed by hot light petroleum (b. p. 50—60°), and finally crystallised from benzene as colourless crystals, m. p. 206° (yellow-orange melt) [Found: C, 90·1; H, 5·2%; *M* (Rast), 365. $C_{28}H_{20}O$ requires C, 90·3; H, 5·4%; *M*, 372]. 2′ : 2′-*Diphenylanthrone*-9-spiro-1′-cyclo*propane* is soluble in hot benzene, but difficultly soluble in cold ethyl alcohol, and gives an orange colour with concentrated sulphuric acid.

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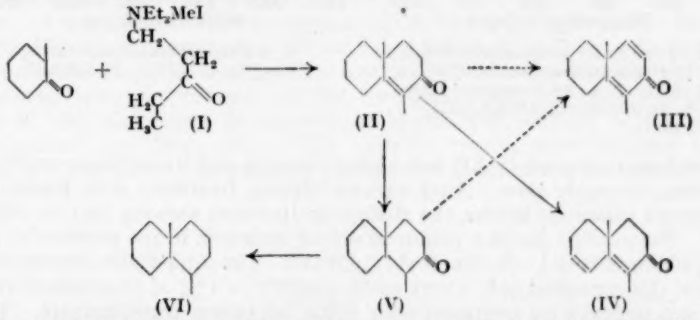
263. *Experiments on the Synthesis of Santonin. Part II.* The Preparation of Compounds containing the Dienone System present in Santonin.*

By F. D. Gunstone and R. M. Heggie.

Attempts to prepare 2 : 5 : 6 : 7 : 8 : 10-hexahydro-2-keto-1 : 10-dimethylnaphthalene (III) from the 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10-octahydro-ketone (II) or the decahydro-ketone (V) have failed although the hexahydro-10-monomethyl-ketone (VII) was prepared by the methods attempted for the conversion of (V) into (III). Condensation of 2-methyl*cyclo*hexanone with ethyl ethynyl ketone has given (III) in small yield.

Having prepared the lactone of α-(2-hydroxy-3-keto*cyclo*hexyl)propionic acid [formula (IV) of Part I *] we turned our attention to the dienone system present in santonin, and this paper describes the attempts to prepare 2 : 5 : 6 : 7 : 8 : 10-hexahydro-2-keto-1 : 10-dimethylnaphthalene (III).

Propionyl chloride condense with ethylene in presence of aluminium chloride in chloroform, giving 1-chloropentan-3-one (McMahon, Roper, Untermohlen, Hasek, Harris, and Brant, *J. Amer. Chem. Soc.*, 1948, **70**, 2971), which with diethylamine (Adamson, McQuillin, Robinson, and Simonsen, *J.*, 1937, 1576) and then methyl iodide (Wilds and Shunk, *J. Amer. Chem. Soc.*, 1943, **65**, 469) gave 1-diethylaminopentan-3-one methiodide (I). Condensation of this with 2-methyl*cyclo*hexanone by the method of du Feu, McQuillin, and Robinson (*J.*, 1937, 53) yielded 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10-octahydro-2-keto-1 : 10-dimethylnaphthalene (II).



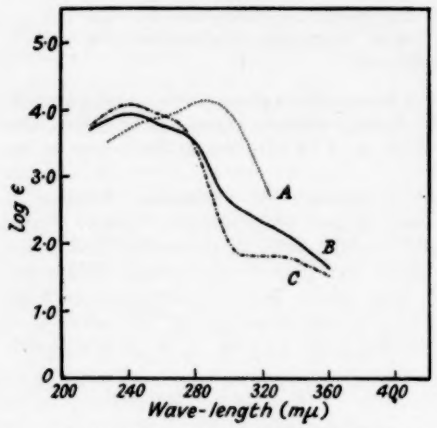
It was hoped that the mono-unsaturated product (II) would yield the required dienone (III) by reaction with *N*-bromosuccinimide and subsequent dehydrobromination. The carbonyl derivatives thus obtained had the required molecular formulæ but their spectra showed the ketone to be (IV) rather than (III); this was not without precedent since similar reactions in the steroid series yield this extended dienone system (cf. Djerassi, *Chem. Reviews*, 1948, **43**, 271). Attempts were then made to add bromine to (II) in the hope that the dibromide would react with *N*-bromosuccinimide and then yield (III) by subsequent loss of one molecule each of hydrogen bromide and bromine (cf. Plattner, Heusser, and Segre, *Helv. Chim. Acta*, 1948, **31**, 249): however, spontaneous dehydrobromination occurred during the initial addition and the product was again (IV). Compounds containing the crossed conjugated dienone system present in (III) absorb at *ca.* 240 mμ (log ε *ca.* 4·1) (Ruzicka, Cohen, Furter, and van der Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735; Woodward and Singh, *J. Amer. Chem. Soc.*, 1950, **72**, 494; Woodward, *ibid.*, 1940, **62**, 1208; Djerassi and Ryan, *ibid.*, 1949, **71**, 1000) whilst compounds in which the extended dienone system (IV) occurs absorb at *ca.* 280 mμ (log ε *ca.* 4·1) (Evans and Gillam, *J.*, 1945, 432; Djerassi and Ryan, *loc. cit.*, Birch, Murray, and Smith, *J.*, 1951, 1945). The product from these reactions had a high absorption

* Part I, *J.*, 1952, 1354.

band (see Fig. 1) at 286 mμ (log ε 4·13) and an inflexion at 249 mμ (log ε 3·83), indicating that the product was mainly (IV) but possibly contained an impurity which gave rise to the inflexion.

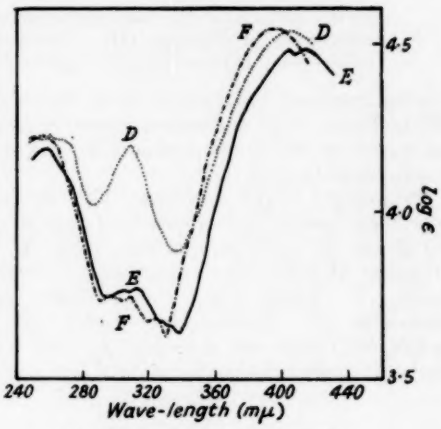
Catalytic hydrogenation of santonin gives dihydrosantonin (Bargellini, *Atti R. Accad. Lincei*, 1912, **22**, 443) which is an analogue of (II). Efforts to repeat this result with palladium–charcoal or Raney nickel, however, yielded almost entirely tetra- and hexahydrosantonin respectively.

FIG. 1.



A, 2 : 3 : 4 : 5 : 6 : 10-*Hexahydro*-2-*keto*-1 : 10-*dimethylnaphthalene* (IV).
B, 2 : 5 : 6 : 7 : 8 : 10-*Hexahydro*-2-*keto*-1 : 10-*dimethylnaphthalene* (III).
C, *Santonin*.

FIG. 2.



2 : 4-*Dinitrophenylhydrazones of*: *D*, (IV); *E*, (III); *F*, *Santonin*.

The condensation product (II) was highly coloured and its reduction with palladium–charcoal was extremely slow. After various failures, treatment with Raney nickel was found to give a colourless ketone, the absorption spectrum showing that no reduction had occurred. The purified product readily absorbed hydrogen in the presence of palladium–charcoal yielding 2-keto-1 : 10-dimethyldecalin (V). The ultra-violet absorption spectrum showed that this contained only a very small quantity (<1%) of unsaturated ketone, most of which was removed by treatment with dilute potassium permanganate. This ketone was reduced by the Clemmensen procedure to *cis*-1 : 10-dimethyldecalin (VI) (Linstead, Millidge, and Walpole, *J.*, 1937, 1140; Ruzicka, Koolhaas, and Wind, *Helv. Chim. Acta*, 1931, **14**, 1151, 1171).

It was hoped that bromination-dehydrobromination of (V) might result in the introduction of double bonds first into the 3 : 4-position and only then into the 1 : 9-position, yielding (III). The experiments and results are shown in the Table. The products from reaction of *N*-bromosuccinimide (1 mol.) and subsequent dehydro-

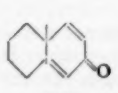
Products obtained by bromination-dehydrobromination (pyridine or collidine) of (V).

Brominating agent	Yield (g.) [1]	$\lambda_{max.}$ (mμ) (log ε) in ethanol	
$(CH_2{\cdot}CO)_2NBr$ (1 mol.) (*a*)	0·51	245 (3·74)	285 (3·12)
(*b*)	0·55	238 (3·64)	285 (3·06)
„ (2 mols.) (*a*)	0·50	232·5 (3·86)	280 (3·59)
(*b*)	0·30	231 (3·89)	289 (3·63)
Br–AcOH (2 mols.)	0·38	222 (3·93) [2]	293 (3·89)
Br–CCl_4 (2 mols.)	0·34	230 (3·90)	300 (3·47)
Br–AcOH (3 mols.)	0·13	226 (3·59)	287 (3·82)
$(CH_2{\cdot}CO)_2NBr$ (2 mols.) [3]	0·06	230 (3·77)	288 (4·05)

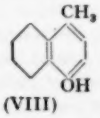
[1] Yield from 1 g. of starting material. [2] Inflexion at 245 mμ (log ε 3·83). [3] Experiment carried out on (II).

bromination had absorption bands at 245 and 285 mμ. The former is close to the value expected from the dienone (V) or the monounsaturated ketone (II), but repetition of the experiment gave a lower value (238 mμ). This suggested that the product was actually a variable mixture [probably of the Δ^3- (225 ± 5 mμ; cf. Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123) and the $\Delta^{1(9)}$-compound (248 mμ)]. The absorption band at 285 mμ indicated the presence of more unsaturated compounds. 3-Keto-steroids with the *cis*-configuration about rings A and B are known to brominate in the 4-position [1-position in (V)] (Djerassi and Scholtz, *Experientia*, 1947, **3**, 107), and since (V) has been shown to have the *cis*-configuration it is possible that bromination has taken place partly at the 1- and partly at the 3-position. Bromination with 2 mols. of *N*-bromosuccinimide might yield the 1 : 3-dibromo-compound as precursor of the required dienone. In fact bromination with 2 mols. of *N*-bromosuccinimide or of bromine in acetic acid or carbon tetrachloride solution again gave mixtures. The absorption band of high wave-length (280—300 mμ) is characteristic of the system CH:CH·CH:CH·CO and may be due to the presence of the dienone (IV) or the 1(9) : 3 : 7-trienone, which could result if the 1-bromo-compound suffered spontaneous dehydrobromination. The absorption at lower wave-length (222—232 mμ) is probably due to one or more of the $\Delta^{1(9)}$ and Δ^3-monounsaturated ketones and the 1(9) : 3-dienone. Finally an effort was made to prepare the 1(9) : 3 : 7-trienone from (II) and from (V) but whilst the absorption band at higher wave-lengths was augmented the product, obtained in low yield, was probably still a mixture.

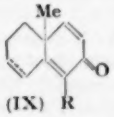
Some of these methods, which have failed to yield the required dienone, are known to yield the system when applied to analogous systems in the sterol series (see Fieser and Fieser, "Natural Products related to Phenanthrene," 3rd edn., 1949, New York). This difference may be due to some peculiarity in the chemistry of the steroids or to the presence of the 1-methyl group (4-methyl in the sterol molecule). Whilst this work was in progress the monomethyl compound (VII) was prepared by Woodward and Singh (*J. Amer. Chem. Soc.*, 1950, **72**, 494) by other methods. We have now prepared (VII) by methods analogous to those already described. It appears then that failure of these methods when applied to (V) is connected with the presence of the 1-methyl group. 2-Keto-10-methyldecalin (du Feu *et al.*, *loc. cit.*), when brominated in acetic acid solution, and subsequently dehydrobrominated (collidine), gave (VII). Similar results were obtained in carbon tetrachloride solution and less satisfactory results with *N*-bromosuccinimide.



(VII)



(VIII)



(IX)

Paranjape, Phalnikar, Bhide, and Nargund (*Rasayanam*, 1943, **1**, 233; *Chem. Abstr.*, 1944, **38**, 4266) also claim to have prepared (VII). The structure of their product depended on the characterisation of the acid-rearrangement product as 5 : 6 : 7 : 8-tetrahydro-4-methyl-2-naphthol. Woodward and Singh (*loc. cit.*), however, have shown that (VII) yields (VIII) on rearrangement and we have confirmed this. It appears from the work of Woodward and Singh (*loc. cit.*) and also of Djerassi *et al.* (*J. Amer. Chem. Soc.*, 1951, **73**, 990) that the nature of the dienone–phenol rearrangement product of compounds containing the structure (IX) depends (*a*) on whether R is H or alkyl and (*b*) on the presence or absence of an additional conjugated double bond in the adjacent ring as shown in (IX). It is not clear what happens when there is no angular methyl group or additional double bond and when R = H. Galinovsky (*Ber.*, 1943, **76**, 230) however has shown that bromination and subsequent dehydrobromination of β-tetralone afford directly β-tetralol. We have confirmed Galinovsky's observation, thus showing that the Woodward–Singh type of rearrangement, which would yield α-tetralol, does not apply in this case.

The methods used by Woodward and Singh (*loc. cit.*) to prepare 2 : 5 : 6 : 7 : 8 : 10-hexahydro-2-keto-10-methylnaphthalene involved (*a*) condensation of 2-formyl-2-methyl-*cyclo*hexanone with acetone in the presence of piperidine acetate (cf. Paranjape *et al.*, *loc. cit.*, and Wilds and Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1715) and (*b*) condensation

of 2-methyl*cyclo*hexanone with ethynyl methyl ketone in the presence of sodium hydride. Condensation of 2-formyl-2-methyl*cyclo*hexanone with ethyl methyl ketone gave a fraction which may have contained (III). This was obtained, however, in very small yield and was possibly a mixture of position isomers. Paranjape *et al.* (*loc. cit.*) claim to have obtained (III) by this method but in view of other criticisms made concerning this work (see p. 1439 and especially Wilds and Djerassi, *loc. cit.*) little reliance can be placed on this.

By the use of previously described methods (Heilbron, Jones, and Weedon, *J.*, 1945, 81; Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39) the hitherto unknown ethyl ethynyl ketone has been prepared. It condensed with 2-methyl*cyclo*hexanone in the presence of sodamide to give a liquid, albeit in low yield, having the properties expected of the desired dienone (III). Hydrogenation of the product afforded a liquid ketone, which gave the 2 : 4-dinitrophenylhydrazone of (V), thus proving that the compound has the correct skeletal structure. Two ethylenic linkages are indicated by the quantitative hydrogenation and by analysis of the 2 : 4-dinitrophenylhydrazone. The position of these double bonds is clearly shown to be as in (III) from the absorption spectra (see Figs. 1 and 2) of the ketone and of its 2 : 4-dinitrophenylhydrazone. The dinitrophenylhydrazone obviously differs from that of (IV). We have not yet been able to obtain any solid tetralol from the alkali-soluble liquid resulting from the acid rearrangement of (III).

This work is being continued.

Experimental

M. p.s are uncorrected. Absorption spectra were determined with a Unicam quartz spectrophotometer, ethanol or chloroform being used as solvent.

1-*Diethylaminopentan*-3-*one Methiodide* (I).—Propionyl chloride and ethylene reacted in the presence of aluminium chloride in chloroform solution (McMahon *et al.*, *loc. cit.*) to give 1-chloropentan-3-one (48%), b. p. 43—47°/3 mm., n_D^{15} 1·4461 (lit., n_D^{20} 1·4361), and thence 1-carbamyl-3-ethylpyrazoline, m. p. 94° (picrate, m. p. 132—134°) (Maire, *Bull. Soc. chim.*, 1908, **3**, 272, gives 96° and 137° respectively). The chloro-ketone and diethylamine (Adamson *et al.*, *loc. cit.*) yielded 1-diethylaminopentan-3-one (80%), b. p. 85—89°/17 mm., n_D^{16} 1·4441 (semicarbazone, m. p. 97—99°; picrate, m. p. 76—78°; Blaise and Maire, *Bull. Soc. chim.*, 1908, **3**, 543, report 100° and 78° respectively), with an equal weight of methyl iodide (cf. Wilds and Shunk, *loc. cit.*), this afforded the methiodide (I) (92%), which was used without further purification.

The initial condensation, effected in excess of propionyl chloride as solvent, gave ethyl vinyl ketone (69%).

2 : 3 : 4 : 5 : 6 : 8 : 10-*Octahydro*-2-*keto*-1 : 10-*dimethylnaphthalene* (II).—2-Methyl*cyclo*hexanone (99 g.), sodamide (18·4 g.), and ether (150 ml.) were stirred for 4 hours at room temperature in a stream of dry nitrogen. 1-Diethylaminopentan-3-one methiodide (135 g.) in ethanol (60 ml.) was added gradually and stirring continued for 4 hours at room temperature and for 2 hours at the b. p. After addition of dilute hydrochloric acid the solution was extracted (ether), dried, and distilled. The octahydroketonaphthalene (II) 37 g. (46%), b p. 99—100°/1 mm., thus obtained was purified by stirring it with Raney nickel in ethanol for 30 minutes and then redistilling it; n_D^{20} 1·5260 and an absorption max. at 248 mμ (log ε 4·14), inflexion at 290 mμ (log ε 2·27) in ethanol, were then observed. The 2 : 4-*dinitrophenylhydrazone* had m. p. 198—199°, scarlet plates from ethanol (Found: C, 60·2; H, 6·1; N, 15·9. $C_{18}H_{22}O_4N_4$ requires C, 60·3; H, 6·2; N, 15·6%), absorption max. at 260 (log ε 4·28) and 394 mμ (log ε 4·47) and inflexion at 296 mμ (log ε 4·06) in chloroform. The *semicarbazone* had m. p. 203—204°, colourless prisms from ethanol [Found: C, 66·3; H, 9·1; N, 17·9. $C_{13}H_{21}ON_3$ requires C, 66·4; H, 9·0; N, 17·9%], absorption max. at 271 mμ (log ε 4·47) in ethanol.

Bromination of (II).—(a) *N-Bromosuccinimide.* *N*-Bromosuccinimide (4·45 g.) was added to a solution of the octahydro-ketone (4·45 g.) in carbon tetrachloride (25 ml.) and the mixture refluxed for 30 minutes. Succinimide (2·41 g.) was removed from the cold solution, as was the solvent, and the residue refluxed with pyridine (10 ml.) for 2 hours. The product was 2 : 3 : 4 : 5 : 6 : 10-hexahydro-2-keto-1 : 10-dimethylnaphthalene (2·53 g., 58%), b. p. 106—108°/1 mm., n_D^{20} 1·5590 [2 : 4-*dinitrophenylhydrazone*, m. p. 216°, dark red plates from acetic acid (Found: C, 60·3; H, 5·9; N, 15·6. $C_{18}H_{20}O_4N_4$ requires C, 60·7; H, 5·7; N, 15·7%), absorption max. at 251, 261, 311, and 407 mμ (log ε 4·22, 4·22, 4·19, and 4·53 respectively) and inflexion at 272 mμ (log ε 4·20) in chloroform; semicarbazone, m. p. 216—217°, absorption max. at 300 mμ (log ε 4·54) in ethanol].

(b) *Bromine.* Bromine (1 ml.) in carbon tetrachloride (10 ml.) was added to a cooled, stirred solution of the octahydro-ketone (3·56 g.) in the same solvent (50 ml.). The temperature slowly rose to room temperature (5—6 hours), the solvent was removed and the residue on distillation afforded the above hexahydro-ketone (2 g., 55%), b. p. 118—126°/1·5 mm. [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 214°; *semicarbazone*, m. p. and mixed m. p. 212—213° (Found: C, 67·1; H, 8·2; N, 18·0. $C_{13}H_{19}ON_3$ requires C, 66·9; H, 8·2; N, 18·0%)].

2-*Keto*-1 : 10-*dimethyldecalin* (V).—The octahydro-2-keto-1 : 10-dimethylnaphthalene (II) (20 g.) was hydrogenated (palladium–charcoal–ethanol), 2·42 l. of hydrogen being absorbed at N.T.P. (theory, 2·51 l.). The solvent and catalyst were removed and the residue was distilled. The distillate (19·13 g., 95%), b. p. 90—91°/0·9 mm., n_D^{19} 1·4961, was purified by occasional shaking with 0·1N-potassium permanganate (400 ml.) during 2 hours. After redistillation 2-keto-1 : 10-dimethyldecalin (85%), b. p. 76—78°/0·5 mm., n_D^{19} 1·4945, was obtained; it gave a yellow 2 : 4-*dinitrophenylhydrazone*, m. p. 186°, from ethanol (Found: C, 59·9; H, 6·6. $C_{18}H_{24}O_4N_4$ requires C, 60·0; H, 6·7%), and a *semicarbazone*, m. p. 189—190°, (plates from ethanol (Found: C, 66·0; H, 9·5; N, 17·7. $C_{13}H_{23}ON_3$ requires C, 65·8; H, 9·8; N, 17·7%).

cis-1 : 10-*Dimethyldecalin* (VI).—2-Keto-1 : 10-dimethyldecalin (4 g.) in toluene (10 ml.) was heated under reflux for 30 hours with zinc (12 g.), water (7·5 ml.) and concentrated hydrochloric acid (17·5 ml. plus 5 × 5 ml. added during refluxing). The reaction mixture after dilution and extraction gave *cis*-1 : 10-dimethyldecalin, b. p. 98—99°/15 mm., n_D^{20} 1·4848. These properties were hardly changed after the material had been heated with dilute potassium permanganate solution and distilled over sodium, *viz.*, b. p. 85—90°/12 mm., (bath-temp.) n_D^{16} 1·4849 (Linstead, Millidge, and Walpole, *J.*, 1937, 1140, give b. p. 84—85°/10 mm., n_D^{16} 1·4787, and Ruzicka *et al.*, *Helv. Chim. Acta*, 1931, **14**, 1151, 1171, give b. p. 85°/12 mm., n_D^{20} 1·4812) (Found: C, 86·7; H, 13·0. Calc. for $C_{12}H_{22}$: C, 86·7; H, 13·3%).

trans-1 : 10-*Dimethyldecalin*.—1 G. each of *cis*-1 : 10-dimethyldecalin and aluminium chloride were left together in a desiccator for 2 days. Dilute hydrochloric acid was then added and the *trans*-form extracted and distilled. It (0·63 g.) had b. p. 86—88°/14 mm. and n_D^{22} 1·4691. The treatment with aluminium chloride was repeated and the product, distilled from sodium, then had b. p. 76—78°/11 mm. (bath-temp.), n_D^{18} 1·4690 (Linstead *et al.*, and Ruzicka *et al.*, *loc. cit.*, give 76—78°/10 mm., n_D^{15} 1·4658 and 77—78°/12 mm., n_D^{20} 1·4659 respectively) (Found: C, 86·6; H, 13·1%).

Bromination-Dehydrobromination of 2-*Keto*-1 : 10-*dimethyldecalin* (V). *General Procedure.*—*N*-Bromosuccinimide was added to a solution of 2-keto-1 : 10-dimethyldecalin in carbon tetrachloride and the mixture refluxed until reaction was complete. Succinimide was removed from the cold solution, followed by the solvent, and the residue, after dehydrobromination by refluxing pyridine or quinoline, was extracted and distilled. Alternatively 2-keto-1 : 10-dimethyldecalin, dissolved in carbon tetrachloride, was treated with bromine in the same solvent at −5° to +5°, or the saturated ketone dissolved in acetic acid was treated with bromine in acetic acid (with addition of 3—4 drops of a 4N-solution of hydrogen bromide in acetic acid) at room temperature with subsequent heating to 50°. In the last two cases the solvent was next removed under reduced pressure and the bromo-compound dehydrobrominated as above. The product was finally distilled under reduced pressure (boiling range for all products, 65—95°/<1 mm.), and examined spectroscopically in ethanol. The results are summarised in the Table.

2-*Keto*-10-*methyldecalin*.—1-Diethylaminobutan-3-one, prepared by Wilds and Shunk's method (*loc. cit.*), when treated with 2-methyl*cyclo*hexanone in the presence of sodamide, following the directions of du Feu *et al.* (*loc. cit.*), gave 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10-octahydro-2-keto-10-methylnaphthalene (25%) which, when purified by Raney nickel as already described, had b. p. 72—74°/0·2 mm., n_D^{19} 1·5154. This was reduced catalytically (palladium–charcoal) to 2-keto-10-methyldecalin (89%), b. p. 86—90°/1·5 mm., n_D^{15} 1·4922. Some of the solid isomer, m. p. 47—48°, could be crystallised from this liquid mixture of isomers, but the liquid distillate was used in the subsequent experiments. The 2 : 4-dinitrophenylhydrazone had m. p. 113—116°; du Feu *et al.* give 152—152·5° for the derivative obtained from the solid ketone; Woodward and Singh (*loc. cit.*) give 125·5—127° for the derivative obtained from the ketone, itself prepared by an alternative procedure. The latter may be the derivative of another pure isomer or, like ours, the derivative of a mixture of stereoisomers.

2 : 5 : 6 : 7 : 8 : 10-*Hexahydro*-2-*keto*-10-*methylnaphthalene* (VII).—Bromine (5·79 g.) in acetic acid (35 ml.) was added to 2-keto-10-methyldecalin (3 g.) in acetic acid (45 ml.). The colour faded to pale yellow after 15 minutes; the solution was then heated to 50° and left at room temperature for 3 hours. After removal of the solvent under reduced pressure the residue was refluxed with collidine (15 ml.) for 70 minutes and the product extracted.

2 : 5 : 6 : 7 : 8 : 10-Hexahydro-2-keto-10-methylnaphthalene (VII) (1·01 g., 34·5%) was distilled, having b. p. 100—110°/*ca.* 0·9 mm., n_D^{16} 1·5507, absorption max. at 243 mμ (log ε 3·89) in ethanol [Woodward and Singh, *loc. cit.*, give b. p. 123—124°/3 mm., absorption max. at 240 mμ (log ε 4·1)]. Bromination in carbon tetrachloride solution or with *N*-bromosuccinimide gave less pure products but the presence of the required dienone was shown by the isolation of the acid rearrangement product (see below).

Catalytic reduction (palladium–charcoal) afforded 2-keto-10-methyldecalin (82%) (hydrogen uptake, 71 ml. at N.T.P.; theory, 69 ml.) (2 : 4-dinitrophenylhydrazone, m. p. 113—115° alone or mixed with that obtained above).

5 : 6 : 7 : 8-*Tetrahydro-4-methyl-1-naphthol* (VIII).—The foregoing hexahydroketone was converted by Woodward and Singh's method (*loc. cit.*) into the acetate (36%), m. p. 80—81°, and then the tetralol (VIII), m. p. 87·8—88·5°. Woodward and Singh (*loc. cit.*) gave m. p. 82° and 87·5—88·5° respectively.

2-*Formyl*-2-*methyl*cyclo*hexanone* (cf. Sen and Mondal, *J. Indian Chem. Soc.*, 1928, **5**, 609).—2-Formyl*cyclo*hexanone (30 g.) (Auwers, Buschmann, and Heidenreich, *Annalen*, 1924, **435**, 277) was converted into its sodio-derivative by sodium (5·74 g.) in benzene (225 ml.) during 30 hours. The filtered and washed salt was then heated with methyl iodide (46 ml.) and benzene (120 ml.) at 95—100° for 12 hours in a steel bomb. Distillation of the filtered reaction mixture gave 2-formyl-2-methyl*cyclo*hexanone (11·9 g., 36%), b. p. 29—31°/<1 mm., $n_D^{17·5}$ 1·4728 (Cornforth, Cornforth, and Dewar, *Nature*, 1944, **153**, 317, give b. p. 47°/0·05 mm., n_D^{18} 1·4683).

Condensation of 2-*Formyl*-2-*methyl*cyclo*hexanone with Ethyl Methyl Ketone.*—Condensation of 2-formyl-2-methyl*cyclo*hexanone (12 g.) with ethyl methyl ketone (125 ml.) in presence of piperidine acetate by Woodward and Singh's method (*loc. cit.*) gave only 0·35 g. of possible condensation product.

Ethyl Ethynyl Ketone.—Interaction of propaldehyde (116 g.) with sodium acetylide (from 47 g. of sodium) according to the procedure of Heilbron, Jones, and Weedon (*loc. cit.*) gave ethylethynylcarbinol (pent-1-yn-3-ol) (75 g., 45%), b. p. 126—129°/758 mm., n_D^{18} 1·4344 (3 : 5-dinitrobenzoate, m. p. 87°; McGrew and Adams, *J. Amer. Chem. Soc.*, 1937, **59**, 1497, give m. p. 91°). Oxidation (cf. Bowden, Heilbron, Jones, and Weedon, *loc. cit.*) yielded ethyl ethynyl ketone (28 g., 45%), b. p. 105—107°, n_D^{19} 1·4188 [2 : 4-*dinitrophenylhydrazone*, yellow platelets (from ethanol), m. p. 149—150·5° (Found : C, 50·6; H, 4·0; N, 20·6. $C_{11}H_{10}O_4N_4$ requires C, 50·4; H, 3·8; N, 21·4%); p-*nitrophenylhydrazone*, yellow needles (from 50% aqueous methanol), m. p. 97—97·5° (Found : C, 60·8; H, 5·4. $C_{11}H_{11}O_2N_3$ requires C, 60·8; H, 5·1%)].

Catalytic reduction over palladium–charcoal (uptake, 231 ml. at N.T.P.; theor., 273 ml.) gave diethyl ketone, identified as its 2 : 4-dinitrophenylhydrazone.

2 : 5 : 6 : 7 : 8 : 10-*Hexahydro*-2-*keto*-1 : 10-*dimethylnaphthalene* (III).—2-Methyl*cyclo*hexanone (30 g.), sodamide (7·8 g.), and anhydrous ether (200 ml.) were stirred with glass beads in a stream of dry nitrogen for 30 hours, extra ether being added to replace that lost by evaporation. Ethyl ethynyl ketone (16·4 g.) in anhydrous ether (50 ml.) was then added gradually with stirring which was continued for 4 hours at 0° and for 6 hours at room temperature. The reaction mixture, decomposed in the cold with 2N-hydrochloric acid, and extracted with ether, gave on distillation a fraction which redistilled at 108—110°/1 mm. (1·79 g., 5%, equiv. to 7·6% calc. on unrecovered 2-methyl*cyclo*hexanone). This was the desired hexahydro-2-keto-1 : 10-dimethylnaphthalene (III), n_D^{20} 1·5322 [2 : 4-*dinitrophenylhydrazone*, dark red plates (from *n*-butanol), m. p. 238—239° (Found : C, 60·4; H, 5·5; N, 15·9. $C_{18}H_{20}O_4N_4$ requires C, 60·7; H, 5·7; N, 15·7%)]. It (0·5 g.) was reduced catalytically (palladium–charcoal; uptake, 109 ml. at N.T.P.; theor., 127 ml.) to 2-keto-1 : 10-dimethyldecalin, b. p. 75—85°/0·5 mm., n_D^{20} 1·4915 (2 : 4-dinitrophenylhydrazone, m. p. 180—181° raised to 184—186° when mixed with a previous sample of m. p. 183—185°).

[With J. R. Davidson.] ar-2-*Tetralol from* 2-*Decalone* (cf. Galinovsky, *loc. cit.*).—2-Decalone (1·11 g.) (du Feu *et al.*, *loc. cit.*) was treated with bromine in acetic acid as already described and subsequently with collidine. The alkali-soluble portion of the product solidified after distillation [150—160°/8 mm. (bath-temp.)] and after crystallisation from light petroleum (b. p. 60—80°) melted at 59·5—60°; its benzoate had m. p. 93—94°. For β-tetralol and its benzoate m. p.s 61—62° and 96° respectively are recorded.

We are indebted to the D.S.I.R. for a Maintenance Allowance to one of us (R. M. H.) and to Mr. J. M. L. Cameron and Miss R. H. Kennaway for the microanalyses.

University of Glasgow. [*Received, December 20th*, 1951.]

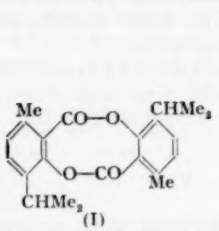
264. *Eight- and Higher-membered Ring Compounds. Part VI.** cis-*Di- and Tri-o-thymotides.*

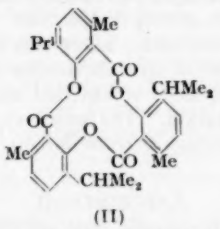
By Wilson Baker, B. Gilbert, and W. D. Ollis.

Dehydration of *o*-thymotic acid by various reagents gives *cis*-di-*o*-thymotide and tri-*o*-thymotide; higher cyclic anhydro-derivatives (cf. the salicylides and cresotides) are not formed. These compounds were described previously as isomeric di-*o*-thymotides. Their reactions with alkali and with benzylamine have been investigated. Tri-*o*-thymotide frequently crystallises with solvent of crystallisation; such solvents include light petroleum, *n*-hexane, and benzene.

Previous papers in this series (Parts II and III, *J.*, 1951, 202, 210) have described cyclic anhydro-derivatives of salicylic and of three of the cresotic acids. It was shown that, contrary to previous claims, only one dianhydro-derivative existed in each case, and that the second supposed isomer was, again in each case, a trianhydro-derivative. In view of these facts, it was clearly desirable to reinvestigate the two thymotides, derived from *o*-thymotic acid (2-hydroxy-6-methyl-3-*iso*propylbenzoic acid), which had been described by Spallino and Provenzal (*Gazzetta*, 1909, **39**, II, 325) as isomeric dithymotides (I). As already reported in a footnote to Part II (*loc. cit.*), these have also been found to be dithymotide (I) and trithymotide (II) containing an eight- and a twelve-membered ring respectively.

Spallino and Provenzal, in a reinvestigation of earlier work by Naquet (*Bull. Soc. chim.*, 1865, [ii], **4**, 93, 98), studied the action of phosphoric anhydride and of phosphorus oxychloride on *o*-thymotic acid in boiling xylene. In each case they obtained two anhydro-derivatives, which after crystallisation from light petroleum had m. p. 209° and 174°, the former being formed in larger yield. Cryoscopic molecular weight determinations in benzene


(I)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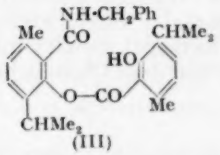
(III)

and phenol gave values in approximate agreement with the dimeric formula. Later, Lespagnol and Lupas (*ibid.*, 1937, [v], **4**, 542) reported that the action of heat on a mixture of *o*-thymotic acid, thymol, and acetic anhydride, followed by distillation, gave only the dithymotide, m. p. 212°.

In repeating the work of Spallino and Provenzal, we confirmed the production of two thymotides. They were separated by fractional crystallisation and by hand sorting, giving di-*o*-thymotide, m. p. 207° (12%), identical with the compound, m. p. 209°, described previously, and a second compound, m. p. 172° (decomp.) (from light petroleum), which was similar to Spallino and Provenzal's "dithymotide," m. p. 174°. The latter compound, however, contains light petroleum which is lost at 160°/1 mm., giving solvent-free material, m. p. 217° (decomp.), which has proved to be tri-*o*-thymotide. This previously undetected solvent of crystallisation undoubtedly led to the incorrect molecular-weight determinations by Spallino and Provenzal. The adduct must clearly be of the clathrate type (see Palin and Powell, *J.*, 1948, 815, and later papers by Powell *et al.*).

The structures of di-*o*-thymotide (I) and tri-*o*-thymotide (II) have been established by analysis, ebullioscopic molecular-weight determination, alkaline hydrolysis, and reaction with benzylamine. The *o*-thymotides are very much more stable than the corresponding

* Part V, *J.*, 1951, 1118.

salicylides and cresotides. They are unaffected by boiling 95% acetic acid, and are only very slowly hydrolysed by dilute aqueous sodium hydroxide; both these reagents cause rapid hydrolysis of *cis*-disalicylide and the *cis*-dicresotides (see Parts II and III). Alkaline hydrolysis of both thymotides was effected, however, under more vigorous conditions, giving *o*-thymotic acid, and reaction with excess of benzylamine gave *N*-benzyl-*o*-thymotamide. Reaction of *cis*-di-*o*-thymotide with half an equivalent of benzylamine gave *N*-benzyl-*O*-*o*-thymotoyl-*o*-thymotamide (III).

The dipole moments of di- (6·63 D) and tri-*o*-thymotide (4·13 D), determined by Dr. L. E. Sutton and Mr. M. F. Saxby of the Physical Chemistry Laboratory, Oxford (forthcoming publication; see also Edgerley and Sutton, *J.*, 1951, 1069), show that di-*o*-thymotide, like disalicylide and the dicresotides, has the *cis*-configuration and that tri-*o*-thymotide has a constellation similar to that proposed for trisalicylide (2·95 D) and tri-*o*-cresotide (4·28 D). The three *o*-thymotide residues are arranged approximately on the faces of a triangular-based pyramid (see photograph facing p. 1070, *J.*, 1951). Steric factors probably account for the marked stability towards hydrolysis of *cis*-di-*o*-thymotide and of tri-*o*-thymotide, compared with the corresponding salicylides and cresotides. In this connection it may be noticed that tri-*o*-cresotide is much more stable to alkali than is trisalicylide.

We have also investigated other methods for the dehydration of *o*-thymotic acid that had been used previously for the preparation of salicylides and cresotides. The action of phosphorus oxychloride on *o*-thymotic acid gave *cis*-di- and tri-*o*-thymotides in 8% and 36% yields respectively. A careful search failed to reveal any higher cyclic anhydro-derivatives, whereas salicylic and cresotic acids yield tetramers and, in two cases, hexamers with this reagent. Low-pressure distillation of *O*-acetyl-*o*-thymotic acid, a method which has been used for the preparation of the lower salicylides and cresotides, gave *cis*-di-*o*-thymotide (39%) and tri-*o*-thymotide (2·5%).*

Tri-*o*-thymotide forms crystal complexes with a wide variety of solvents (see experimental section). The adducts with light petroleum, *n*-hexane, and ethanol are remarkably stable; they dissociate only very slowly below 160°. The other adducts investigated decompose more readily, but incompletely, below this temperature.

The crystalline unsolvated form of tri-*o*-thymotide is obtained by crystallisation from methanol, but careful exclusion of seeds of solvated material is necessary, and even then some methanol complex may separate. The unsolvated compound may also crystallise partly unchanged from light petroleum or from dioxan.

Experimental

M. p.s are uncorrected. Molecular weights were determined in the Menzies–Wright apparatus as described in Part II, p. 208. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

o-Thymotic Acid.—The method described by Spallino and Provenzal (*loc. cit.*) gives a 35% yield. By increasing the reaction time from 5 to 20 hours, the yield of once recrystallised *o*-thymotic acid was raised to 79%.

Action of Phosphoric Anhydride on o-Thymotic Acid (cis-*Di-o-thymotide and Tri-o-thymotide*). —A mixture of *o*-thymotic acid (15 g.), phosphoric anhydride (15 g.), and xylene (78 c.c.) was boiled under reflux for 5 hours. The cooled mixture was shaken with water, then with 5% aqueous sodium hydrogen carbonate (50 c.c.), and again with water, dried ($MgSO_4$), and evaporated, leaving a crystalline residue, m. p. 130—170° (10·9 g.). This was heated with ethanol (100 c.c.) for ½ hour and the mixture filtered whilst hot, leaving the crude, sparingly soluble *tri-o-thymotide* (2·2 g.) as colourless crystals, m. p. 177—184°. The filtrate on cooling deposited a mixture of di-*o*-thymotide and a smaller quantity of the tri-*o*-thymotide–ethanol complex.

* [*Note added in proof*, 3.3.52.] *X*-Ray crystallographical examination of the *n*-hexane and benzene complexes of trithymotide is being carried out by H. M. Powell and A. C. D. Newman of the Chemical Crystallography Laboratory, Oxford. Enantiomorphous forms of trithymotide resembling right- and left-handed three-bladed propellors are possible, and resolution occurs during crystallisation. Single crystals of the benzene complex give optically active solutions which racemise fairly rapidly. This is the first case of the detection of optical activity due to enantiomorphous constellations of molecules of this type. Details of this work will be published later.

This mixture was partially separated by hand, and the remainder of the material was subjected to a repetition of the above process, eventually giving *cis*-di-*o*-thymotide (1·6 g.) and the tri-*o*-thymotide–ethanol complex (0·5 g.). The di-*o*-thymotide, after recrystallisation from light petroleum (b. p. 80—100°; 100 c.c.) and twice from ethanol (50 c.c.), was obtained as colourless needles (0·9 g.), m. p. 207° (Found: C, 74·7; H, 7·0%; *M*, ebullioscopic in benzene, 353; ebullioscopic in chloroform, 353. Calc. for $C_{22}H_{24}O_4$: C, 75·0; H, 6·9%; *M*, 352).

The crude tri-*o*-thymotide and tri-*o*-thymotide–ethanol complex were recrystallised separately from dioxan (20 c.c./g.) and then from light petroleum (b. p. 80—100°), giving in each case the *tri-o-thymotide–light petroleum* complex as a mixture of long and slender, or short and thick, hexagonal prisms, both having m. p. (and mixed m. p.) 172° (decomp.). Both forms of the light petroleum complex lost the solvent when heated for 5 hours at 160°/1 mm., giving *tri-o-thymotide* as a microcrystalline powder, m. p. 217° (decomp.) [Found: C, 74·9; H, 7·2%; *M* (ebullioscopic) in benzene 522, in chloroform 538, in carbon tetrachloride 515. $C_{33}H_{36}O_6$ requires C, 75·0; H, 6·9%; *M*, 528].

Action of Phosphorus Oxychloride on o-*Thymotic Acid* (cis-*Di-o-thymotide and Tri-o-thymotide*).—A mixture of *o*-thymotic acid (20 g.), redistilled phosphorus oxychloride (9·4 c.c.), and dry xylene (114 c.c.) was heated on a steam-bath for 12 hours. The cooled mixture was shaken with water and the solid, crude tri-*o*-thymotide–xylene complex (1·9 g.; m. p. 169—180°) collected. The xylene layer of the filtrate was separated and deposited more of the tri-*o*-thymotide–xylene complex (2·5 g.) on being kept. The final xylene filtrate was then washed with 5% aqueous sodium hydrogen carbonate (2 × 50 c.c.), then with water, and evaporated, leaving a partly crystalline residue (9·6 g.). This was separated as described above into *cis*-di-*o*-thymotide (1·4 g.) and the tri-*o*-thymotide–ethanol complex (3·4 g.). The *cis*-di-*o*-thymotide, after 3 further recrystallisations from ethanol and then from light petroleum (b. p. 80—100°), was obtained as colourless needles, m. p. 207°. The tri-*o*-thymotide–ethanol complex was recrystallised from dioxan and then from methanol (50 c.c./g.), eventually giving tri-*o*-thymotide (3·5 g.) as fine, colourless needles, m. p. 217° (decomp.) (Found: C, 74·8; H, 6·7%), and the *tri-o-thymotide–methanol* complex (0·9 g.), m. p. 175—185° (decomp.).

O-*Acetyl-o-thymotic Acid*.—Lespagnol and Bar (*Bull. Soc. chim.*, 1938, [v], **5**, 1360) obtained *O*-acetyl-*o*-thymotic acid as a colourless oil by the action of acetic anhydride on *o*-thymotic acid in the presence of sodium acetate. *o*-Thymotic acid (20 g., 0·13 mole), acetic anhydride (33 g., 0·33 mole), and concentrated sulphuric acid (0·5 g.) were heated at 55—60° for ½ hour and then at 90° for 3 hours. The cooled solution was poured into water (500 c.c.) and stirred for 5 hours, and the resulting oil was dissolved in chloroform (200 c.c.) and extracted with 5% aqueous sodium hydrogen carbonate (150 c.c.). The aqueous layer was washed with chloroform and acidified, yielding an oil which was extracted with chloroform (150 c.c.), dried ($MgSO_4$), and evaporated, giving *O*-acetyl-*o*-thymotic acid as a colourless oil (13·5 g.) (Found: equiv., 243. Calc. for $C_{13}H_{15}O_2{\cdot}CO_2H$: equiv., 236). The use of pyridine in place of sulphuric acid gave a similar result.

Action of Heat on O-*Acetyl-o-thymotic Acid* (cis-*Di-o-thymotide and Tri-o-thymotide*. Cf. Lespagnol and Lupas, *loc. cit.*).—*O*-Acetyl-*o*-thymotic acid (17 g.) was slowly distilled at 18·5 mm. pressure, using an air-bath, the temperature of which was gradually raised to 300° (cf. preparation of disalicylide, Part II). Brisk evolution of acetic acid occurred at about 150°, and a solid distillate (8·9 g.) was collected mainly between 230° and 250° (internal temp.). This was dissolved in chloroform (50 c.c.), washed with 2N-sodium hydroxide (2 × 50 c.c.), then with water, dried ($MgSO_4$), and evaporated, leaving a crystalline residue (8·2 g.). This was dissolved in hot ethanol and worked up as before, giving crude *cis*-di-*o*-thymotide (5·0 g.) and the tri-*o*-thymotide–ethanol complex (0·32 g.). After two recrystallisations from ethanol (200 c.c.), the *cis*-di-*o*-thymotide was obtained as needles (4·2 g.), m. p. 207°. The tri-*o*-thymotide–ethanol complex was recrystallised 3 times from light petroleum (b. p. 80—100°; 5 c.c.), giving the light petroleum complex (0·28 g.), m. p. 172° (decomp.).

Alkaline Hydrolysis of the o-*Thymotides*.—The *o*-thymotides could only be hydrolysed by concentrated aqueous sodium hydroxide. *cis*-Di-*o*-thymotide (0·10 g.) was heated at 95—100° with (initially 50%) aqueous sodium hydroxide (1 c.c.) in a nickel vessel for 3 days. Water (75 c.c.) was added, and the solution filtered from unchanged *cis*-di-*o*-thymotide (0·2 mg.) and acidified, precipitating *o*-thymotic acid (0·102 g., 93%), m. p. and mixed m. p. 122—123°.

Tri-*o*-thymotide (50 mg.) and 10% ethanolic potassium hydroxide (5 c.c.) were heated under reflux for 9 hours, freed from ethanol under diminished pressure, treated with water (5 c.c.), and acidified, giving *o*-thymotic acid (50 mg., 91%), m. p. and mixed m. p. 122—123°.

Reaction of the o-*Thymotides with Excess of Benzylamine* (N-*Benzyl-o-thymotamide*).—*cis*-

Di- and tri-*o*-thymotide were each boiled under reflux for 3 hours with excess of benzylamine and a trace of ammonium chloride, cooled, and poured into 2N-hydrochloric acid. The solid was collected and recrystallised from aqueous methanol (1 : 1), giving in each case *N-benzyl-o-thymotamide* as colourless needles, m. p. 92·5° (Found : C, 76·3; H, 6·9; N, 5·0. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·4; N, 5·0%). The yields were 96% from *cis*-di-*o*-thymotide and 92% from tri-*o*-thymotide. The *N*-benzyl-*o*-thymotamide obtained by this method was identical (mixed m. p.) with a specimen prepared from methyl thymotate and excess of benzylamine under the same conditions.

N-*Benzyl*-O-o-*thymotoyl*-o-*thymotamide* (III).—*cis*-Di-*o*-thymotide (0·5 g.) and benzylamine (0·15 g.), dissolved in dry xylene (25 c.c.), were boiled under reflux for 40 hours. The xylene was then removed, leaving an oil which crystallised when kept. One recrystallisation from alcohol gave a product (0·068 g.; m. p. 202—204°) which, after purification, was identified as unchanged *cis*-di-*o*-thymotide. The residue obtained by evaporation of the mother-liquor was recrystallised 6 times from methanol (5 c.c.)–water (1 c.c.), giving N-*benzyl*-O-o-*thymotoyl*-o-*thymotamide* as needles (0·045 g.), m. p. 163° (Found : C, 75·9; H, 7·7; N, 3·2. $C_{29}H_{33}O_4N$ requires C, 75·8; H, 7·2; N, 3·1%).

Crystal Complexes of Tri-o-thymotide.—Crystallisation of tri-*o*-thymotide from a variety of solvents gives *complexes* containing solvent of crystallisation (see Table). Except in the case of the light petroleum and *n*-hexane complexes, slow cooling (*ca.* 5°/hr.) of the hot solution of tri-*o*-thymotide is necessary to obtain a homogeneous product free from unsolvated tri-*o*-thymotide. The methanol complex has not been obtained free from unsolvated material. Loss in weight was determined, in general, at 160°/1 mm. The approximate times, in hours, necessary for complete dissociation were : light petroleum, 3; *n*-hexane, 4½; ethanol, 13, followed by 6 at 178°; methanol, 4; *m*- and *p*-xylene, some loss occurs at 18°, and at 100° approximately half a molecule of solvent is lost in 4 hours; complete loss occurs after a further 2 hours at 160°.

Crystalline complexes formed by tri-o-thymotide.

Component	M. p.* (dissociation)	Mol. ratio, component/tri-*o*-thymotide.	Found (required in parentheses): Carbon, %	Hydrogen, %	Loss in wt., %
Light petroleum (b. p. 80—100°) †	172°	½	76·0 (75·8)	7·6 (7·6)	8·7 (8·7)
n-Hexane	173	½	75·3 (75·6)	7·4 (7·6)	7·6 (7·5)
Ethanol	178	½	73·6 (74·0)	7·2 (7·1)	4·7 (4·2)
Methanol	175	<½	—	—	2·3 (2·9) ‡
m-Xylene	172	½	—	—	13·5 (13·1)
p-Xylene	159	1	—	—	16·3 (16·7)

* M. p.s are those at which melting begins. It usually occurs over a range of 10—20°.

† Largely heptanes. The calculated analytical figures are those for a heptane complex. The determinations were made on the slender, prismatic form.

‡ The required loss in weight (2·9%) is for a methanol complex containing half a molecule of methanol per molecule of trimer. The complex used for this determination was non-homogeneous and satisfactory analytical figures could not be obtained. Analysis of the *m*- and *p*-xylene complexes was not possible owing to their instability.

Complexes are also formed with benzene, carbon tetrachloride, chloroform, and dioxan.

THE UNIVERSITY, BRISTOL.

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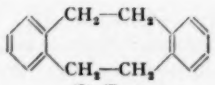
265. *Eight- and Higher-membered Ring Compounds. Part VII.* The Lactone of 2′-Hydroxydibenzyl-2-Carboxylic Acid.*

By Wilson Baker, W. D. Ollis, and T. S. Zealley.

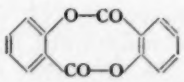
Compounds of the type of di-*o*-xylylene (I) might possibly exist in both *cis*- and *trans*-forms; di-*o*-xylylene is the *trans*-molecule, whilst disalicylide (II) possesses the *cis*-configuration. We have now prepared the 8-membered lactone of 2′-hydroxydibenzyl-2-carboxylic acid (III) in the hope that two stereoisomerides might be isolated, but only one lactone is formed and its dipole moment shows that it has the *cis*-configuration. The lactone is prepared from the hydroxy-acid by a variety of methods; *e.g.*, reaction with trifluoroacetic anhydride gives a 95% yield. Dehydration of *m*- and *p*-hydroxybenzoic acids has given only material of high molecular weight.

Considerable interest attaches to the stereochemistry of compounds of the type of di-*o*-xylylene (I) in which two benzene rings are fused symmetrically to an 8-membered ring. It is possible that such molecules (in which any or all of the methylene groups may be replaced by suitable bivalent atoms or groups) might be isolable in two stereoisomeric forms, a rigid (in some cases centrosymmetrical) *trans*-form (chair), and a mobile, folded, *cis*-form (trough). Interconversion of the *cis*- and the *trans*-form without bond breaking necessitates passage through a very highly strained configuration. The *cis*-form can pass without strain into a second *cis*-form folded in the opposite way, and these two would be identical, *e.g.*, in the case of di-*o*-xylylene, or optical enantiomorphs, *e.g.*, in the case of disalicylide (II); intermediate between the two *cis*-forms is a skew form which, like the folded *cis*-forms, has no centre of symmetry.

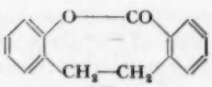
The possibility of stereoisomerism of this type was first suggested by Höhn (see Richter-Anschütz, "Chemie der Kohlenstoff-Verbindungen," 1935, Vol. II, 2, 392) to account for the existence of two supposed stereoisomerides of disalicylide, and it was discussed in some detail by Baker, Banks, Lyon, and Mann (*J.*, 1945, 27). It has been shown, however (Part II, Baker, Ollis, and Zealley, *J.*, 1951, 202) that one of the supposed disalicylides was trisalicylide, and the disalicylide has been proved by dipole-moment measurement to possess the folded *cis*-configuration (Edgerley and Sutton, *J.*, 1951, 1069). Contrary to previous claims, it has also been shown that only one stereoisomeride exists of di-*o*-, di-*m*-, and di-*p*-cresotide (Part III, Baker, Gilbert, Ollis, and Zealley, *J.*, 1951, 210) and of dithymotide (Part VI, Baker, Gilbert, and Ollis, preceding paper), and that these all have the *cis*-configuration (Edgerley and Sutton, *loc. cit.*; Saxby and Sutton, forthcoming publication). On the other hand, Davidson (quoted in *J.*, 1945, 30) has shown by *X*-ray methods that di-*o*-xylylene (dibenzo*cyclo*octa-1 : 5-diene) (I) has a centre of symmetry, and is, therefore, the *trans*-isomeride; and it may be presumed that molecules of this kind will exist in the *trans*-form unless they possess some constraining feature; for example, in disalicylide, resonance in the lactone groupings causes the molecule to take up the *cis*-form as this is the only form in which the lactone group can be planar (see discussion in Part II, *loc. cit.*).



(I) *Trans*



(II) *Cis*



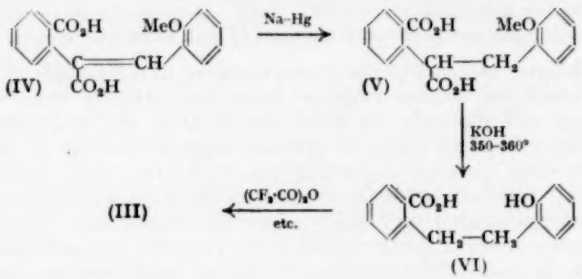
(III)

In considering which molecules of the type under discussion are most likely to exist in stereoisomeric forms, we have thought it worth while to synthesise the lactone of 2′-hydroxydibenzyl-2-carboxylic acid (III), in which the dimethylene group would favour the *trans*- and the lactone group the *cis*-configuration. Synthesis of the lactone was finally achieved, but only of one form, and this has been shown, by its high dipole moment (4·09 D), to possess the extreme folded configuration (Saxby and Sutton, forthcoming publication).

* Part VI, preceding paper.

Clearly the resonance energy requirements of the lactone grouping control the stereochemistry of the molecule.

The synthesis of the lactone (III) was carried out as follows. Reaction of either homophthalic acid or its anhydride with *o*-methoxybenzaldehyde in presence of acetic anhydride and sodium acetate gave a mixture of the *cis*- and the *trans*-isomer of *o*-methoxybenzylidenehomophthalic acid (IV). Reduction of each stereoisomer with sodium amalgam gave the same saturated acid (V), so that for preparative purposes they need not be separated. The acid (V) when fused for a few minutes with potassium hydroxide at 350—360° underwent simultaneous decarboxylation and demethylation, giving the acid (VI) in 57% yield; the structure of (VI) is proved by oxidation to phthalic acid and by formation of an acetyl derivative.

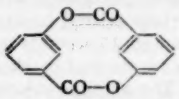


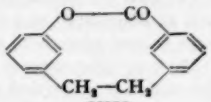
The dehydration of the acid (VI) to give the 8-membered lactone (III) presents several points of interest, and is a reaction involving the rigid-group principle in large-ring formation which was discussed in Part I of this series (Baker, McOmie, and Ollis, *J.*, 1951, 200). When heated with acetic anhydride and anhydrous sodium acetate the acid yielded simply the *O*-acetyl derivative, in contrast with the formation of a seven-membered lactone when 2-carboxy-2′-hydroxydiphenylmethane is treated with acetic anhydride (see following paper). When this acetyl derivative was heated at atmospheric pressure it lost acetic acid, and the sublimed product yielded some 10% of the lactone (III); this method is analogous to one of those employed in preparing di- and tri-salicylides and -cresotides from the *O*-acetyl-salicylic and -cresotic acids. Yields of the lactone (III) of 40—60% were obtained by dehydration of the acid (VI) with phosphoric anhydride in benzene, with phosphorus oxychloride in benzene, or with thionyl chloride followed by diethylaniline (cf. formation of salicylides and cresotides). By far the best reagent is trifluoroacetic anhydride (Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2977), which when employed in benzene solution gave the lactone in 95% yield. The lactones (III) prepared by all these methods were identical, and no indication could be obtained of the formation of a stereoisomer. The lactone (III) is readily hydrolysed by alkali, being much less stable in this respect than the closely related disalicylide, but, whereas disalicylide is rapidly hydrolysed by boiling with dilute acetic acid, the lactone (III) is almost unaffected by this treatment.

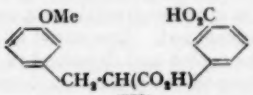
In an attempt to prepare the 8-membered cyclic ether corresponding to (III), having CH_2 in place of CO, the acid (VI) was reduced with lithium aluminium hydride to 2-hydroxy-2′-hydroxymethyldibenzyl, but the replacement of the aliphatic hydroxyl group by chlorine and subsequent cyclisation have not been successfully carried out.

In view of the successful synthesis of di-*m*-xylylene and of tri-*p*-xylylene by the Wurtz–Fittig reaction (Part IV, Baker, McOmie, and Norman, *J.*, 1951, 1114) we have investigated the dehydration of *m*- and *p*-hydroxybenzoic acids by the various methods which have been used for the preparation of cyclic di- and higher-anhydro-derivatives of *o*-hydroxybenzoic acids (see Parts II and III, *loc. cit.*). In no case, however, was anything but material of high molecular weight obtained, and the failure in the *m*-series to form the 10-membered lactide (VII) is probably due to the fact that the ester bridges are some 0·2 Å shorter than the dimethylene bridges of di-*m*-xylylene, so that steric interaction

between the two internal CH groups would be greater even than in di-*m*-xylylene (see Part IV, *loc. cit.*, p. 1115).


(VII)


(VIII)


(IX)

The synthesis of the analogous lactone (VIII), which is more likely to be capable of formation than the lactide (VII), was therefore attempted by a series of reactions parallel to those used for the preparation of the lactone (III). *m*-Methoxybenzaldehyde was condensed with *iso*homophthalic acid and the product reduced by sodium amalgam to the acid (IX), but alkaline decarboxylation and demethylation could not be effected as with the isomeride (V), and only the demethylated dicarboxylic acid was isolated. Decarboxylation of (IX) with copper chromite was not successful.

Experimental

M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and by Mr. W. M. Eno, Bristol.

cis- *and* trans-o-*Methoxybenzylidenehomophthalic Acids* (α-o'-*Carboxyphenyl*-2-*methoxycinnamic Acids*) (IV) —A mixture of homophthalic acid (2·2 g.) (Whitmore and Cooney, *J. Amer. Chem. Soc.*, 1944, **66**, 1239) or homophthalic anhydride (see Price, Lewis, and Meister, *ibid.*, 1939, **61**, 2762) (2·0 g.), *o*-methoxybenzaldehyde (2·01 g.), fused sodium acetate (1·01 g.), and redistilled acetic anhydride (5·04 g.) was heated at 160° for 3·5 hours, cooled, and poured into 2N-sodium hydroxide (100 c.c.). After being shaken at 100° for 15 minutes, the mixture was filtered, giving a filtrate *A* and a yellow solid (0·9 g.). This solid was heated with more 2N-sodium hydroxide until it dissolved (solution *B*).

Filtrate (*A*) was washed with ether, acidified, and extracted with ether. The extract, after drying ($MgSO_4$), yielded a gum, which was crystallised from benzene, and the solid (2·4 g., 65%), m. p. 195°, was recrystallised from ethyl acetate or aqueous ethanol, giving an *acid* (*isomer A*) (2·05 g.) as colourless rhombs, m. p. 210—211° (rapid heating) [Found: C, 68·1; H, 4·8; OMe, 10·9%; equiv., 149. $C_{14}H_8(OMe)(CO_2H)_2$ requires C, 68·4; H, 4·7; OMe, 10·4%; equiv., 149].

Solution *B* similarly gave a solid (0·36 g., 10%), m. p. 208—210°, which after three recrystallisations from methanol gave *isomer B* (0·21 g.) as colourless prisms, m. p. 218—221° (dependent on rate of heating) (Found: C, 68·3; H, 5·2; OMe, 10·0%; equiv., 162). These isomeric acids gave different ultra-violet light extinction curves in ethanol, but after irradiation for 12 hours with ultra-violet light the two solutions gave identical curves.

In some experiments conducted at 180°, isomer *B* was not isolated, and when the benzene mother-liquors of the first crystallisation of isomer *A* were concentrated, a crystalline solid (0·26 g.), m. p. 270—275°, separated which, after recrystallisation from ethanol or *n*-amyl acetate, gave a *substance* (0·14 g.) as colourless needles, m. p. 275—277° (decomp.) (Found: C, 75·5; H, 4·8; OMe, 8·0%; equiv., 410. $C_{25}H_{18}O_5$ requires C, 75·3; H, 4·6; OMe, 7·8%; equiv., 398). This compound was not further investigated.

α-o-*Methoxybenzylhomophthalic Acid* (α-o-*Carboxyphenyl*-β-o'-*methoxyphenylpropionic Acid*) (V).—(*a*) *o*-Methoxybenzylidenehomophthalic acid (isomer *A*) (2·66 g.), 2% sodium amalgam (250 g.), and water (100 c.c.) were left at room temperature for 24 hours with occasional shaking. Acidification gave a precipitate of the *acid* (V) (2·33 g., 88%), m. p. 165—166°, which, after recrystallisation from aqueous ethanol, formed colourless needles, m. p. 166° (Found: C, 68·1; H, 5·2. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%).

(*b*) Similarly reduction of the isomer *B* gave the acid (V) (yield 86%), m. p. and mixed m. p. 166°.

(*c*) Homophthalic acid (11·1 g.), *o*-methoxybenzaldehyde (10 g.), anhydrous sodium acetate (6 g.), and acetic anhydride (24 c.c.) were heated at 160—170° for 2·25 hours, and the product boiled for 1 hour with 30% aqueous sodium hydroxide (150 c.c.) and poured into water (1 l.). Acidification and cooling to 0° gave the mixed acids (IV) (17·4 g., 95%) which were reduced with 2·5% sodium amalgam and water (500 c.c.), giving finally the acid (V) (15·9 g., 91%), m. p. 165—166°.

2'-Hydroxydibenzyl-2-carboxylic Acid (VI).—Many experiments showed that the following method was the most satisfactory.

α-*o*-Methoxybenzylhomophthalic acid (V) (5·0 g.) was added to fused potassium hydroxide (30 g.) in a nickel crucible in a metal-bath at 350—360° and the mixture stirred continuously with a nickel rod. The initial effervescence ceased after 3·25 minutes and 15 seconds later the melt was cooled and dissolved in water (250 c.c.) (the success of this reaction is markedly dependent upon the precise conditions under which it is carried out). The alkaline solution was filtered and acidified, giving crystalline material (2·8 g., 70%), m. p. 133—137°. Recrystallisation from carbon tetrachloride (50 c.c.) or benzene gave *2'-hydroxydibenzyl-2-carboxylic acid* (VI) (2·3 g., 57%) as colourless needles, m. p. 140—141° (Found: C, 74·4; H, 6·1%; equiv., 255. $C_{14}H_{13}O{\cdot}CO_2H$ requires C, 74·3; H, 5·8%; equiv., 242). This acid sublimed unchanged at 180—200°/16 mm.

Oxidation of this acid (46 mg.) with a hot saturated solution of potassium permanganate in acetone gave phthalic acid (23 mg.).

2'-Acetoxydibenzyl-2-carboxylic Acid.—2'-Hydroxydibenzyl-2-carboxylic acid (VI) (1 g.), acetic anhydride (10 c.c.), and fused sodium acetate (0·25 g.) were boiled for 2 hours, cooled, and poured into water. The solid (0·985 g., 87%), m. p. 95—102°, was recrystallised from benzene–light petroleum (b. p. 60—80°), giving *2'-acetoxydibenzyl-2-carboxylic acid* as colourless needles, m. p. 123° (Found: C, 71·8; H, 5·6%; equiv., 298. $C_{16}H_{15}O_3{\cdot}CO_2H$ requires C, 71·8; H, 5·7%; equiv., 284). This acid sublimed unchanged at 180—190°/1 mm.

Lactone of 2'-Hydroxydibenzyl-2-carboxylic Acid (III).—(a) *Action of thionyl chloride and diethylaniline on 2'-hydroxydibenzyl-2-carboxylic acid* (VI). A mixture of 2'-hydroxydibenzyl-2-carboxylic acid (0·25 g.), anhydrous benzene (20 c.c.), and purified thionyl chloride (0·16 g.) was kept at 45—50° for 1 hour and boiled under reflux for ½ hour. Diethylaniline (0·3 g.) was then added and after a further 2 hours' boiling the solvents were removed and the residue was shaken with ether and 2N-hydrochloric acid. The ethereal layer was washed with 2N-sodium hydroxide, dried ($MgSO_4$), and evaporated, yielding a dark residue (196 mg.) which gave a colourless sublimate (78 mg., 35%) at 160—170°/16 mm. Crystallisation from light petroleum (b. p. 100—120°) then gave the *lactone* (III) as colourless rhombs, m. p. 115—116° [Found: C, 80·6; H, 5·4%; *M*(Rast), 208; *M* (ebullioscopic in benzene), 228. $C_{15}H_{12}O_2$ requires C, 80·3; H, 5·4%; *M*, 224]. The yield fell to 22% after 12 hours' heating.

(b) *Action of trifluoroacetic anhydride on 2'-hydroxydibenzyl-2-carboxylic acid* (VI). Trifluoroacetic anhydride (6 c.c.) was added to a solution of the acid (4·55 g.) in anhydrous benzene (300 c.c.) at 35°, and after 1 hour at room temperature the solution was heated under reflux for a further hour, then washed with aqueous sodium carbonate and with water, and dried ($MgSO_4$), and the benzene removed under diminished pressure. The residue was dissolved in hot ether (100 c.c.), and this solution, after concentration, was left in a refrigerator overnight, giving the lactone (III) (4·0 g.; 95%), m. p. and mixed m. p. 115—116°.

The yield was not so good in the absence of a solvent; *e.g.*, the acid (VI) (0·5 g.) and trifluoroacetic anhydride (1·5 g.), after 30 minutes' heating under reflux, gave the lactone in 65% yield.

(c) *Action of heat on 2'-acetoxydibenzyl-2-carboxylic acid.* The acetoxy-acid was heated at 250—260° at atmospheric pressure, acetic acid being evolved. The residue was then sublimed at 250°/3 mm., and the sublimate, after being washed with 2N-sodium hydroxide, gave the lactone (III) (yield, *ca.* 10%), m. p. and mixed m. p. 114°.

(d) *Reaction of 2'-hydroxydibenzyl-2-carboxylic acid* (VI) *with phosphorus oxychloride in benzene.* The acid (1·5 g.), redistilled phosphorus oxychloride (1·0 g.), and anhydrous benzene (25 c.c.) were heated under reflux for 3 days. The decanted benzene solution, after being washed with 10% aqueous sodium carbonate and dried ($MgSO_4$), gave a crystalline residue (1·02 g., 63%) of the lactone (III), m. p. and mixed m. p. 115° after recrystallisation from ether.

(e) *Reaction of 2'-hydroxydibenzyl-2-carboxylic acid* (VI) *with phosphoric anhydride.* The acid (1·0 g.), phosphoric anhydride (4·0 g.), and anhydrous benzene (200 c.c.) were heated under reflux for 4 hours, cooled, and filtered. After being washed with 10% aqueous sodium carbonate and dried ($MgSO_4$), the benzene solution gave a solid residue (0·52 g., m. p. 95—110°) which, after crystallisation from ether, gave the lactone (III) (0·5 g.), m. p. and mixed m. p. 115°.

Alkaline Hydrolysis of the Lactone of 2'-Hydroxydibenzyl-2-carboxylic Acid (III).—The lactone (III) (115 mg.) and 2N-aqueous sodium hydroxide (10 c.c.) were boiled until a clear solution was obtained (5 minutes). Acidification then gave 2'-hydroxydibenzyl-2-carboxylic acid (VI) (115 mg., 93%), m. p. and mixed m. p. 140—141°. At room temperature a solution of the

lactone in ethanol was hydrolysed in ½ hour to the extent of 19% with 10% aqueous sodium carbonate, and 70% with 10% aqueous sodium hydroxide.

2-Hydroxy-2'-hydroxymethyldibenzyl.—2'-Hydroxydibenzyl-2-carboxylic acid (VI) (2 g.) in anhydrous ether (70 c.c.) was added dropwise to a stirred boiling solution of lithium aluminium hydride (1 g.) in anhydrous ether (100 c.c.) in an atmosphere of nitrogen. Water and dilute hydrochloric acid were added, and the dried ($MgSO_4$) ethereal layer and extracts gave a residue which was crystallised from aqueous ethanol. *2-Hydroxy-2'-hydroxymethyldibenzyl* separated as fine needles (1·44 g., 76%), m. p. 109·5° (Found: C, 78·9; H, 7·2. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·0%).

m-*Methoxybenzylidenehomoisophthalic Acid* (α-m'-*Carboxyphenyl*-3-*methoxycinnamic Acid*).—A mixture of homo*iso*phthalic acid (3·2 g.) [prepared from *m*-cyanobenzyl cyanide (Reinglas, *Ber.*, 1891, **24**, 2416) by hydrolysis with dilute sulphuric acid (Kommpa and Hirn, *Ber.*, 1903, **36**, 3611)], *m*-methoxybenzaldehyde (2·86 g.), fused potassium acetate (1·77 g.), and acetic anhydride (7·45 g.) was heated under reflux (oil-bath at 170°) for 4 hours, cooled, diluted with water, and extracted with ether. The extract gave a product which was then dissolved in aqueous sodium carbonate, shaken with ethyl acetate and ether, and acidified. The solid (4·8 g., 90%) was recrystallised from aqueous acetic acid giving the *acid* (3 g.) as yellow rhombs, m. p. 216° (Found: C, 68·5; H, 4·8. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%).

α-m-*Methoxybenzylhomoisophthalic Acid* (α-m-*Carboxyphenyl*-β-m-*methoxyphenylpropionic Acid*) (IX).—The foregoing acid (2·37 g.), 2% sodium amalgam (230 g.), and water (90 c.c.) were left for 6 days. Acidification precipitated the *acid* (IX) (2·28 g., 95%), m. p. 158—160°; after recrystallisation from aqueous acetic acid it was obtained as colourless microscopic crystals, m. p. 162—163° (Found: C, 68·3; H, 5·5. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%). This acid was not decarboxylated when heated in quinoline with or without copper chromite. Attempted decarboxylation by fusion with alkali gave the following result.

α-m-*Hydroxybenzylhomoisophthalic Acid* (α-m-*Carboxyphenyl*-β-m-*hydroxyphenylpropionic Acid*).—The acid (IX) (0·5 g.) was added to stirred, fused potassium hydroxide (3 g.) in a nickel crucible heated in a metal bath at 290°, and after 95 seconds it was rapidly cooled. The reaction mixture was dissolved in water, filtered, acidified, and extracted with ether (45 c.c.). The extract yielded the *hydroxy-acid* which crystallised from dilute hydrochloric acid as white rhombs (0·176 g., 37%), m. p. 170° [Found: C, 66·5; H, 4·9; OMe, 0·0%; equiv., 151. $C_{14}H_{12}O(CO_2H)_2$ requires C, 67·0; H, 4·9%; equiv., 143].

3 : 3-*Dibenzylphthalide.*—An ethereal solution (100 c.c.) of benzylmagnesium bromide prepared from benzyl bromide (13·6 g.) and magnesium (1·35 g.) was added (½ hour) to a boiling, stirred solution of phthalic anhydride (7·5 g.) in anhydrous benzene (150 c.c.) in an atmosphere of nitrogen. After a further 2·5 hours' heating, the mixture was poured on ice and 2N-hydrochloric acid (200 c.c.), the benzene layer separated, and the aqueous layer extracted with ether. The combined extracts were washed with 2N-sodium carbonate (acidification of which gave phthalic acid, 5·5 g.), dried ($MgSO_4$), and evaporated, leaving a residue (6·0 g.) which was crystallised from benzene. **3 : 3-***Dibenzylphthalide* forms needles, m. p. 205° (Found: C, 84·3; H, 5·7. $C_{22}H_{18}O_2$ requires C, 84·1; H, 5·8%).

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THE UNIVERSITY, BRISTOL. [*Received, December 27th*, 1951.]

266. *Eight- and Higher-membered Ring Compounds. Part VIII.* Anhydro-derivatives of 2-Carboxy-2′-hydroxybenzophenone and of 2-Carboxy-2′-hydroxydiphenylmethane.*

By Wilson Baker, D. Clark, W. D. Ollis, and T. S. Zealley.

2-Carboxy-2′-hydroxybenzophenone and 2-carboxy-2′-hydroxy-5′-methylbenzophenone (I; R = H and Me) yield the 7-membered lactones (II; R = H and Me) by the action of acetic anhydride, but other dehydrating agents give the 14-membered lactides (III; R = H and Me). It is suggested that intramolecular hydrogen bonding occurs, which would cause these molecules to take up a configuration unfavourable for lactonisation, but favourable for intermolecular lactide formation. This explanation is supported by the fact that the related acids 2-carboxy-2′-hydroxydiphenylmethane and 2-carboxy-2′-hydroxy-5′-methyldiphenylmethane (VII; R = H and Me), in which similar internal hydrogen bonding cannot occur, give only the 7-membered lactones with all dehydrating agents used.

Examples have been discussed in Parts I—VII of this series (*J.*, 1951, 200, 202, 210, 1114, 1118; preceding papers) illustrating what we have termed the rigid-group principle, namely, the easy formation of large-ring compounds by union of simple units containing rigid groups of atoms. These rigid groups have been present in *o*-xylylene dibromide (Baker, Banks, Lyon, and Mann, *J.*, 1945, 27) and in various *o*-hydroxybenzoic acids (4-membered rigid groups; Parts II, III, and VI), *m*-xylylene dihalides (5-membered rigid groups), *p*-xylylene dihalides (6-membered rigid groups; Part IV), and 2 : 7-bisbromomethylnaphthalene (7-membered rigid groups; Part V). In all these examples intramolecular cyclisation is excluded on stereochemical grounds, and in the last the rigid group extends over two fused benzene rings. The formation of the 8-membered lactone described in Part VII is somewhat different; the hydroxy-acid, 2′-hydroxydibenzyl-2-carboxylic acid, is composed of two directly linked 4-membered rigid groups, but there was the possibility, not realised in fact, that an intermolecular reaction might occur with the formation of a 16-membered lactide.

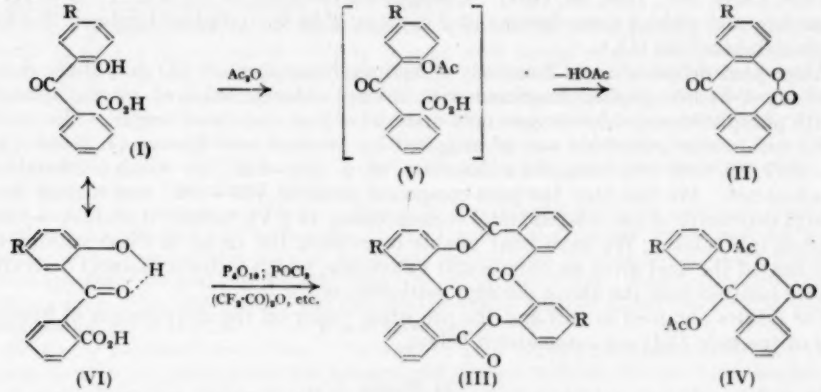
In a further study of the rigid-group principle cases have now been investigated where both intramolecular cyclisation and the production of large-ring compounds by intermolecular condensation could occur. At least one such case is on record; 2 : 2′-dibromodiphenyl, when converted into the Grignard reagent and treated with anhydrous cupric chloride, gives a mixture of diphenylene (dibenzo*cyclo*butadiene) and tetraphenylene (tetrabenzo*cyclo*octatetraene) (Rapson, Shuttleworth, and Niekerk, *J.*, 1943, 326). The same possibilities may be involved in the formation of the higher anhydro-derivatives of *o*-hydroxybenzoic acids. Thus, for example, salicyloylsalicylic acid, $HO{\cdot}C_6H_4{\cdot}CO{\cdot}O{\cdot}C_6H_4{\cdot}CO_2H$, is known to undergo intramolecular cyclisation to disalicylide, and it may be that two molecules could condense to give tetrasalicylide.

The compound first investigated was 2-carboxy-2′-hydroxybenzophenone (I; R = H) which when dehydrated might yield, as the simplest products, either the monomeric 7-membered lactone (II; R = H) or the dimeric 14-membered lactide (III; R = H). When this acid was treated in the cold with acetic anhydride it yielded the lactone (II; R = H) after several hours, but the reaction is base-catalysed and occurred very rapidly in presence of sodium acetate. Other dehydrating agents gave only the lactide (III; R = H); those used were trifluoroacetic anhydride, thionyl chloride followed by treatment with diethylaniline, phosphoric anhydride, and phosphorus oxychloride. The actual yields of the lactide (III; R = H) varied between 30 and 60%; in the case of trifluoroacetic anhydride the yield (32%) was quantitative after allowance for recovered hydroxy-acid.

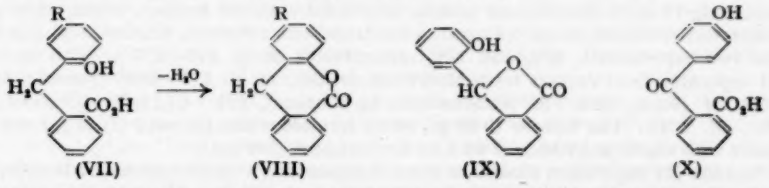
Precisely analogous results were obtained by the dehydration of 2-carboxy-2′-hydroxy-5′-methylbenzophenone (I; R = Me); with cold acetic anhydride it yielded the lactone (II; R = Me), but with the other reagents mentioned it yielded the bimolecular lactide

* Part VII, preceding paper.

(III; R = Me). In some experiments treatment of (I; R = Me) with hot acetic anhydride and sodium acetate yielded the lactone (II; R = Me), but on other occasions it gave the diacetyl derivative of the related lactol, 3-acetoxy-3-(2-acetoxy-5-methylphenyl)phthalide (IV).



In considering the reasons why the action of acetic anhydride on the acids (I) should yield the lactones (II), whilst other methods of dehydration give the lactides (III), it is known that acetic anhydride reacts very rapidly in the cold with *o*-hydroxy-carbonyl compounds to give the *O*-acetyl derivatives. The acids (I) will hence be first converted into the acetyl derivatives (V) (these are too labile to be easily isolated) which then lose acetic acid by a base-catalysed exchange reaction to give the lactones (II). The fact that the acids (I) dissolve only slowly, presumably with chemical change, in acetic anhydride to give solutions which do not at first contain appreciable quantities of the lactone, supports this view that the acetyl derivatives (V) are intermediates. Other dehydrating agents, including doubtless trifluoroacetic anhydride, which probably first forms a mixed anhydride with the carboxyl group (see Bourne, Randles, Tatlow, and Tedder, *Nature*, 1951, **168**, 942), will leave the phenolic group free, and internal hydrogen bonding between the phenolic group and the oxygen atom of the adjacent ketone group will cause the molecule (I) to take up the configuration shown in (VI). This configuration (VI), or any modification derived by rotation of the carboxyphenyl group, is completely unfavourable for intramolecular cyclisation, but two such units [compare (VI) with the left side of formula (III) of the lactide] could clearly unite to give the lactide (III).



In order to test the hypothesis, we have studied the dehydration of the derived 2-carboxy-2′-hydroxydiphenylmethane (VII; R = H) and 2-carboxy-2′-hydroxy-5′-methyldiphenylmethane (VII; R = Me), in which similar hydrogen bonding cannot occur. When treated with any of the dehydrating agents previously mentioned, these acids gave only the 7-membered lactones (VIII; R = H and Me respectively) without trace of 14-membered lactides. This is probably the first case of a hydrogen bond being sterically responsible for the prevention of intramolecular cyclisation, and thereby causing intermolecular reaction with formation of a large ring (for orientation effects of hydrogen bonding see Baker, *J.*, 1934, 1684; Baker and Lothian, *J.*, 1935, 628; 1936, 274).

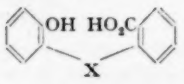
The four lactones (II) and (VIII) undergo rapid hydrolysis with alkali, but the two

lactides (III) are less readily hydrolysed. In all cases the original hydroxy-acids are regenerated.

The acids (VII; R = H or Me) were prepared by reduction of the related keto-acids (I; R = H or Me) with activated zinc dust and aqueous sodium hydroxide (cf. Martin, *J. Amer. Chem. Soc.*, 1936, **58**, 1438). Clemmensen reduction of the acid (I; R = H) was incomplete and yielded the γ-lactone of 2-carboxy-2′-hydroxydiphenylcarbinol (3-*o*-hydroxyphenylphthalide) (IX).

Attempted dehydration of 2-carboxy-4′-hydroxybenzophenone (X) and of the derived 2-carboxy-4′-hydroxydiphenylmethane with thionyl chloride followed by diethylaniline, or with phosphorus oxychloride gave only material of high molecular weight. The reaction of (X) with acetic anhydride was investigated by Orndorff and Murray (*J. Amer. Chem. Soc.*, 1917, **39**, 680) who obtained a diacetate, m. p. 137—140°, for which a formula was not advanced. We find that the pure compound melts at 155—156°, and it must be the diacetyl derivative of the related lactol corresponding to (IV), namely 3-acetoxy-3-*p*-acetoxyphenylphthalide. We have been unable to confirm the claim of these authors that when heated the acid gives its bimolecular anhydride, which yields a diacetyl derivative; we have isolated only the above diacetyl derivative of the lactol.

The results obtained in this and the preceding paper on the dehydration of hydroxy-acids of the type (XI) are summarised below.



(XI)

X=	Ac_2O	$(CF_3{\cdot}CO)_2O$	$SOCl_2$–NPhEt$_2$	P_4O_{10}	$POCl_3$
CH_2	Lactone	Lactone	Lactone	Lactone	Lactone
$CH_2{\cdot}CH_2$	*O*-Acetyl derivative	,,	,,	,,	,,
CO	Lactone	Lactide	Lactide	Lactide	Lactide

Experimental

M. p.s are uncorrected; in cases where they varied with the rate of heating the method described in Part II was used. Molecular weights were determined by the modified Menzies–Wright method also given in Part II. Microanalyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

Lactone (II; R = H) *of 2-Carboxy-2′-hydroxybenzophenone.*—2-Carboxy-2′-hydroxybenzophenone (I; R = H) (0·50 g.; Ullmann and Schmidt, *Ber.*, 1919, **52**, 2107), when stirred with cold acetic anhydride (5 c.c.), dissolved in 7 minutes, giving a solution which did not deposit crystals when seeded with either the lactone (II; R = H) or the acid (I; R = H) (a solution of the calculated amount of lactone in this volume of acetic anhydride is supersaturated). However, after being kept either for 3 hours, or for 2 minutes after addition of anhydrous sodium acetate (2 mg.), the mixture became semi-solid with the lactone, which, after shaking with water to decompose excess of acetic anhydride, was collected, washed, and dried (yield from the two experiments, 87% and 77% respectively; m. p. 176—177°). This *lactone* (II; R = H) separates from carbon tetrachloride in needles, m. p. 179—180° [Found: C, 75·0; H, 4·0%; *M* (Rast), 223; *M* (ebullioscopic in benzene), 224. $C_{14}H_8O_3$ requires C, 75·0; H, 3·6%; *M*, 224]. The lactone (0·89 g., 96%) resulted when the acid (I) (1 g.) was boiled for 2 hours with acetic anhydride (1·95 c.c.) and benzene (100 c.c.).

The lactone (14 mg.) when shaken at room temperature with 2N-sodium hydroxide (1 c.c.) dissolved in ½ hour, and acidification regenerated the acid (I; R = H), m. p. and mixed m. p. 169—171° (95%).

Lactide (III; R = H) *of 2-Carboxy-2′-hydroxybenzophenone.*—Method (*a*) gave a lactide, m. p. 320—322°, whereas the other methods gave a product, m. p. 316°. These m. p.s are not very reliable owing to some decomposition, but the identity of all the specimens was proved by their infra-red spectra and *X*-ray powder photographs. We thank Dr. L. N. Short, Oxford, and Mr. I. S. Loupekine, Bristol, for these measurements.

(a) *Use of trifluoroacetic anhydride.* Trifluoroacetic anhydride (5·7 c.c.; Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2977) was added to 2-carboxy-2′-hydroxybenzophenone (2·0 g.) (I; R = H) in benzene (200 c.c.) at 35° (temporary red coloration). After 2 days the solution was heated on the water-bath for 2½ hours, then concentrated to 2 c.c., and light petroleum

(30 c.c.; b. p. 60—80°) was added. The solid was collected (0·58 g., 32%; m. p. 317—320°) and recrystallised from aqueous acetic acid (100 c.c.), giving the *lactide* of 2-carboxy-2′-hydroxybenzophenone (III; R = H) as hexagonal prisms, m. p. 320—322° [Found: C, 74·8; H, 3·7%; *M* (ebullioscopic in benzene), 468. $C_{28}H_{16}O_6$ requires C, 75·0; H, 3·6%; *M*, 448]. It sublimes unchanged at 240°/0·5 mm. The benzene–light petroleum filtrate yielded unchanged 2-carboxy-2′-hydroxybenzophenone (1·35 g., 68%).

(b) *Use of thionyl chloride and diethylaniline.* The acid (I; R = H) (2 g.), purified thionyl chloride (2 c.c.), and aluminium chloride (2 mg.) were heated at 45—50° for 2 hours, more thionyl chloride (1 c.c.) was added, and heating continued for 1 hour. After evaporation under diminished pressure the residue was heated on a steam-bath for 3 hours with dioxan (10 c.c.) and diethylaniline (3 c.c.) and poured into 0·5N-hydrochloric acid, and the product (1·4 g.; m. p. 305—306°) crystallised from aqueous acetic acid (25 c.c.), giving the lactide (III; R = H) (1·03 g., 56%), m. p. 316° [Found: C, 74·7; H, 3·5%; *M* (ebullioscopic in benzene), 458; *M* (ebullioscopic in chloroform), 446].

(c) *Use of phosphorus oxychloride.* The acid (I; R = H) (0·54 g.) and redistilled phosphorus oxychloride (0·3 c.c.) in benzene (10 c.c.) were heated on the steam-bath for 3 days, benzene (80 c.c.) was added, and the whole was shaken with 2N-sodium carbonate (filtered to remove sparingly soluble sodium salts), then with water, and dried. Evaporation left a residue (0·23 g.; m. p. 260—265°) which was recrystallised from slightly diluted acetic acid (30 c.c.), giving the lactide (0·16 g., 32%), m. p. and mixed m. p. 316°.

(d) *Use of phosphoric anhydride.* The acid (I; R = H) and phosphoric anhydride (3·4 g.) in benzene (110 c.c.) were heated for 5 hours, and the hot solution was decanted, washed with 5% sodium hydrogen carbonate, then with water, and dried. Evaporation left a residue (0·56 g.; m. p. 280—305°) which, after recrystallisation gave the lactide (0·3 g., 31%), m. p. and mixed m. p. 316°.

This lactide (III; R = H) (50 mg.), when boiled with 2N-sodium hydroxide (5 c.c.) for 2 hours, and then acidified, gave the acid (I; R = H) (40 mg.), m. p. and mixed m. p. 168—170°.

Action of Acetic Anhydride on 2-Carboxy-2′-hydroxy-5′-methylbenzophenone (I; R = Me).—(a) *Lactone* (II; R = Me). The acid (I; R = Me) (0·50 g.) (Ullmann and Schmidt, *Ber.*, 1919, **52**, 2102) was ground with acetic anhydride (5 c.c.) at about 30° till dissolution occurred (20 minutes). Seeding with the lactone (II; R = Me) did not cause crystallisation, but after several hours, or immediately after addition of a little anhydrous sodium acetate, the lactone separated. The mixture was shaken with water, and the solid collected, washed, dried (yield 0·44 g.; m. p. 140—143°), and recrystallised from light petroleum (b. p. 80—100°), giving the *lactone* (II; R = Me) as long needles, m. p. 145° [Found: C, 75·2; H, 4·5%; *M* (ebullioscopic in benzene), 240. $C_{15}H_{10}O_3$ requires C, 75·6; H, 4·2%; *M*, 238]. Hydrolysis by boiling the lactone with 2N-sodium hydroxide for ½ minute regenerated the acid (I; R = Me) in 96% yield.

(b) 3-*Acetoxy*-3-(2-*acetoxy*-5-*methylphenyl*)*phthalide* (IV; R = Me). The acid (I; R = Me) (5 g.), acetic anhydride (100 c.c.), and anhydrous sodium acetate (2 g.) were heated on the steam-bath for 2 hours and poured into water, giving a solid (5·7 g.; m. p. *ca.* 150—167°) which was crystallised from carbon tetrachloride (250 c.c.). The *phthalide* (4·1 g.) separated as plates, m. p. 178—179° [Found: C, 66·4; H, 4·8; Ac, 26·9%; *M* (ebullioscopic in benzene), 342. $C_{15}H_{10}O_4Ac_2$ requires C, 66·2; H, 4·8; Ac, 25·3; *M*, 340]. In some apparently similar experiments only the lactone (II; R = Me) was isolated.

Lactide (III; R = Me) *of* 2-*Carboxy*-2′-*hydroxy*-5′-*methylbenzophenone*.—(a) *Use of trifluoroacetic anhydride.* The acid (I; R = Me) (1·45 g.) and trifluoroacetic anhydride (4 c.c.) in benzene (160 c.c.) were kept for 1 hour, boiled for 2½ hours, and then evaporated under diminished pressure. The residue crystallised, giving a solid, m. p. 45°, which may be a mixed anhydride. After this had been heated with pyridine (10 c.c.) on a steam-bath for 2½ hours and poured into 2N-sodium carbonate, the product (0·683 g.; m. p. 287—292°) was triturated with 2N-hydrochloric acid and crystallised from aqueous acetic acid, giving the *lactide* (III; R = Me) (0·65 g., 49%) as prisms, m. p. 294—295° [Found: C, 75·5; H, 4·2%; *M* (ebullioscopic in benzene), 479. $C_{30}H_{20}O_6$ requires C, 75·6; H, 4·2%; *M*, 476].

(b) *Use of thionyl chloride and diethylaniline.* The acid (I; R = Me) gave by reaction with thionyl chloride and then diethylaniline, as described in the case of the acid (I; R = H), the recrystallised lactide (III; R = Me), m. p. and mixed m. p. 295—296°, in 59% yield.

(c) *Use of phosphorus oxychloride.* Dehydration of the acid (I; R = Me) with phosphorus oxychloride, as described for the lower homologue, gave the recrystallised lactide (III; R = Me), m. p. and mixed m. p. 295°, in 45% yield.

(d) *Use of phosphoric anhydride.* The acid (I; R = Me) and phosphoric anhydride gave, as previously described, the lactide (III; R = Me), m. p. and mixed m. p. 295—296°, in 50% yield.

The lactide was completely hydrolysed by boiling it with 2N-sodium hydroxide for 2 hours; acidification yielded the acid (I; R = Me), m. p. and mixed m. p. 194—195°, in 61% yield.

3-o-*Hydroxyphenylphthalide* (IX).—2-Carboxy-2′-hydroxybenzophenone (I; R = H) (1 g.), amalgamated zinc (2·5 g.), concentrated hydrochloric acid (15 c.c.), water (5 c.c.), and toluene (50 c.c.) were boiled under reflux for 24 hours, with the addition after 8 and 16 hours of amalgamated zinc (2 g.) and concentrated hydrochloric acid (10 c.c.). The toluene layer was united with the ethereal extract of the aqueous layer and shaken with 2N-sodium hydroxide, and the alkaline solution was acidified. The resulting oil (0·73 g.), isolated by ether, was crystallised from benzene, giving 3-o-*hydroxyphenylphthalide* (IX) as needles, m. p. 142° or 159° (dimorphic) (Found: C, 74·1; H, 4·3. $C_{14}H_{10}O_3$ requires C, 74·4; H, 4·5%). Although insoluble in cold 10% aqueous sodium carbonate, it dissolves in cold 2N-sodium hydroxide and is recovered unchanged on acidification.

2-*Carboxy-2′-hydroxydiphenylmethane* (VII; R = H).—Zinc dust (2·5 g.) (activated by being shaken with dilute copper sulphate) was boiled with a solution of 2-carboxy-2′-hydroxybenzophenone (1 g.) in 2N-sodium hydroxide (40 c.c.) for 5 hours, and the whole cooled, filtered, and acidified. The solid (0·84 g.; m. p. 121—123°) was crystallised from benzene and then from carbon tetrachloride, giving 2-*carboxy-2′-hydroxydiphenylmethane* (VII; R = H) as needles, m. p. 125° (Found: C, 73·5; H, 5·5%; equiv., 229. $C_{13}H_{11}O{\cdot}CO_2H$ requires C, 73·7; H, 5·3%; equiv., 228).

Lactone (VIII; R = H) *of* 2-*Carboxy-2′-hydroxydiphenylmethane.*—(a) *Use of acetic anhydride.* The acid (VII; R = H) (0·20 g.) was dissolved in cold acetic anhydride (0·5 c.c.) (15 minutes), and fused sodium acetate (2 mg.) was added. After a further 10 minutes, the mixture was shaken with water, and the precipitate (0·16 g.; m. p. 93—96°) crystallised from light petroleum (3 c.c.; b. p. 60—80°). The *lactone* (VIII; R = H) (120 mg.) separated as prisms, m. p. 98—99° [Found: C, 80·1; H, 4·9%; *M* (ebullioscopic in benzene), 209. $C_{14}H_{10}O_2$ requires C, 79·9; H, 4·8%; *M*, 210].

(b) *Use of thionyl chloride and diethylaniline.* The acid (VII; R = H) was converted into the chloride in benzene solution, and then treated with diethylaniline as in previous cases. The lactone (VIII; R = H), obtained in 49% yield, was purified by sublimation (150°/0·5 mm.) and then by crystallisation from light petroleum; it had m. p. and mixed m. p. 98—99°.

(c) *Use of other reagents.* Use of trifluoroacetic anhydride, phosphorus oxychloride, or phosphoric anhydride, as for the analogue, gave the lactone in 75, 51, and 59% yield, respectively, identification being by mixed m. p.s.

This lactone dissolved when heated with 2N-sodium hydroxide (4 minutes), and acidification gave the acid (VI; R = H), m. p. and mixed m. p. 123—124°.

2-*Carboxy-2′-hydroxy-5′-methyldiphenylmethane* (VII; R = Me).—This *acid* was prepared by the reduction of the keto-acid (I; R = Me) (5·3 g.) as in the case of the acid (I; R = H). The product, crystallised from aqueous acetic acid (80 c.c.) and then from carbon tetrachloride (300 c.c.), formed needles (3·75 g.), m. p. 125° (Found: C, 74·4; H, 5·4%; equiv., 262. $C_{14}H_{13}O{\cdot}CO_2H$ requires C, 74·4; H, 5·4%; equiv., 242).

Lactone (VIII; R = Me) *of* 2-*Carboxy-2′-hydroxy-5′-methyldiphenylmethane.*—The methods used were as described for the dehydration of the acid (VII; R = H). Identity of the lactone specimens was proved by mixed m. p. determinations in all cases.

Use of acetic anhydride. 2-Carboxy-2′-hydroxy-5′-methyldiphenylmethane (VII; R = Me) (98 mg.), acetic anhydride (10 c.c.), and sodium acetate (200 mg.) were boiled for 2½ hours, giving the *lactone* (72 mg.) as plates, m. p. 121°, from aqueous ethanol [Found: C, 80·7; H, 5·5%; *M* (ebullioscopic in benzene), 227. $C_{15}H_{12}O_2$ requires C, 80·4; H, 5·4%; *M*, 224].

Trifluoroacetic anhydride, thionyl chloride–diethylaniline, phosphorus oxychloride, and phosphoric anhydride gave yields of 99, 65, 50, and 54% respectively.

Hydrolysis of the lactone by boiling 2N-sodium hydroxide was complete in 25 minutes. Acidification gave the acid (VII; R = Me) (93% yield), m. p. and mixed m. p. 124°.

2-*Carboxy-4′-hydroxydiphenylmethane.*—Reduction of 2-carboxy-4′-hydroxybenzophenone (X) (10 g.; Ullmann and Schmidt, *loc. cit.*) with activated zinc dust and aqueous sodium hydroxide, as in the similar cases described above, gave 2-*carboxy-4′-hydroxydiphenylmethane* (8·75 g.) as needles, m. p. 151°, from slightly diluted acetic acid (Found: C, 73·6; H, 5·3%; equiv., 233. $C_{13}H_{11}O{\cdot}CO_2H$ requires C, 73·7; H, 5·3%; equiv., 228). The *monoacetate* formed rhombs,

m. p. 123—125°, from ethanol (Found: C, 71·2; H, 5·2. $C_{14}H_{11}O_3Ac$ requires C, 71·1; H, 5·2%).

3-*Acetoxy*-3-p-*acetoxyphenylphthalide* (see Orndorff and Murray, *loc. cit.*).—2-Carboxy-4′-hydroxybenzophenone (X) (10 g.; Ullmann and Schmidt, *loc. cit.*) and acetic anhydride (60 c.c.) were heated for 2 hours, concentrated under diminished pressure, and poured into water, and the finally solid product collected (15·3 g.; m. p. 135—145°). Repeated crystallisation from ethanol gave 3-*acetoxy*-3-p-*acetoxyphenylphthalide* as microscopic crystals, m. p. 155—156° [Found: C, 66·0; H, 4·6%; *M* (ebullioscopic in benzene), 330. $C_{18}H_{14}O_6$ requires C, 66·2; H, 4·3%; *M*, 326].

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267. *Reactions in Aqueous Solutions of Sodium Metaperiodate exposed to Artificial Light.*

By FRANK S. H. HEAD and H. A. STANDING.

When dilute solutions of pure sodium metaperiodate are exposed in glass vessels to the enclosed carbon flame-arc they suffer quantitatively complete autoreduction to iodate at a rate convenient for measurement. This is similar to the reaction that occurs much more slowly when metaperiodate solutions are exposed to daylight. When dilute solutions of sodium metaperiodate are exposed in silica vessels to the mercury-in-quartz lamp they suffer autoreduction successively to iodate and iodide. In the presence of air, this is followed by oxidation of iodide ion to iodine, and formation of tri-iodide ion. All these reactions can be followed quantitatively by spectrophotometry.

HEAD (*Nature*, 1950, **165**, 236) reported that dilute solutions of pure sodium metaperiodate are stable in the dark, but suffer autoreduction when exposed to daylight behind glass. The products are sodium iodate and ozonised oxygen, the reaction being eventually quantitatively complete. The absorption spectrum of metaperiodate solutions contains a single band in the wave-length range 200—600 mμ, its maximum being at 220 mμ. Thus the reaction observed by Head occurs under the influence of light of wave-length far removed from that of the absorption maximum. Oertel (*Biochem. Z.*, 1914, **60**, 480) showed that solutions of iodates exposed in silica vessels to the mercury-in-quartz lamp suffer rapid reduction to iodides and oxygen. He did not report results for periodates, but stated that they behave similarly to iodates when similarly irradiated. Presumably, therefore, he observed the reduction of periodates to iodides, but not the formation of iodates as a first stage in the reaction.

The present paper reports more detailed observations of the behaviour of metaperiodate solutions when exposed to artificial light sources richer than daylight in short-wave radiation; these are the enclosed carbon flame-arc and the mercury-in-quartz lamp. The reactions occurring in the system were followed by spectrophotometry.

The carbon flame-arc, enclosed in a glass globe, was surrounded by a heat filter consisting of two concentric glass cylinders forming an annular space through which water circulated. From about 420 mμ upwards the energy distribution in such a source is similar to that in daylight. Owing, however, to the emission bands of the cyanogen radical, which reach their maximum at about 385 mμ, the arc emits radiation of high intensity in the far violet and near ultra-violet that has no counterpart in daylight; much of this radiation is transmitted by the glass globe and heat filter.

The results of exposing 10^{-4}M-sodium metaperiodate solutions, sealed in resistance-glass tubes, at a distance of 9½ inches from the arc centre are shown by the spectral curves of Fig. 1. The upper curve ($\lambda_{max.} = 220$ mμ; $\varepsilon_{max.} = 9{\cdot}8 \times 10^3$) is the absorption curve of pure 10^{-4}M-sodium metaperiodate solution not irradiated. It is in substantial agreement with the absorption measurements on the metaperiodate ion made by Crouthamel, Meek, Martin, and Banks (*J. Amer. Chem. Soc.*, 1949, **71**, 3031). The lowest

curve in Fig. 1 is the absorption curve of pure 10^{-4}M-sodium iodate, which contains no maximum at wave-lengths above 200 mμ; the absorption is relatively low at 220 mμ ($\varepsilon = 1{\cdot}3 \times 10^3$), where the metaperiodate curve attains its maximum. The intermediate curves are those obtained for the 10^{-4}M-metaperiodate solution exposed to the arc for various times from 2 to 96 hours. The irradiation produces a rapid fall in the peak density of the solution, and the spectral curve obtained after the longest exposure is nearly identical with that of 10^{-4}M-sodium iodate. Calculated from the peak densities, the amount of reduction of periodate after various times is as follows:

Time of exposure (hours)	1	2	3	5	15	24
Reduction, %	10	17	24	38	79	90

Spectral curves calculated additively for mixtures of periodate and iodate of the above compositions correspond closely to the experimental curves. The data are not suitable for a precise analysis of the reaction kinetics because the radiation from the arc was not

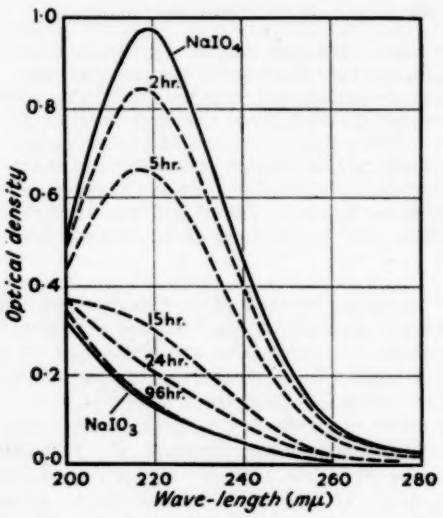


FIG. 1. *Optical densities (1 cm.) of:* 10^{-4}M-$NaIO_4$; 10^{-4}M-$NaIO_3$; *and* 10^{-4}M-$NaIO_4$; *exposed for different times to the enclosed carbon flame arc.*

sufficiently constant; they correspond approximately, however, to a first-order reaction. When a pure 10^{-4}M-solution of iodate was exposed to the arc for 24 hours under the foregoing conditions its absorption spectrum suffered little change.

Quantitatively complete autoreduction of metaperiodate to iodate ion may thus be observed in exposures both to daylight and to the carbon arc. The time necessary for a reduction of 90% when metaperiodate solutions are exposed to direct summer daylight is of the order of 2—3 months. The much higher rate observed in exposures to the arc is no doubt due, not merely to the difference in intensity, but to the fact that the arc emits radiation of wave-length nearer to that of the absorption maximum.

It has been shown in a similar way that complete reduction to iodate occurs when 10^{-4}M-sodium metaperiodate, contained in a closed silica tube, is exposed to the mercury-in-quartz lamp under suitable conditions, and that the reaction is then relatively rapid. The source was a commercial high-pressure mercury lamp deprived of its glass bulb (Mercra, 125 watts). The change from the spectrum of metaperiodate to that of iodate was practically complete in 15 minutes at 3½ inches from the source. When, however, the duration and intensity of the irradiation were greatly increased, further changes occurred in the spectral absorption curve of the solution, and these were partly due to the further reduction of iodate to iodide. This is the reaction reported by Oertel, who did not observe the first stage in the reduction of the periodate ion, which occurs at a much greater rate

than the subsequent reduction to iodide. It is unlikely that he could have done so by means of the chemical methods of analysis employed by him. As will be shown, spectrophotometric methods are particularly suitable for revealing the complicated series of successive reactions occurring in aqueous metaperiodate solutions exposed to short-wave radiation in the presence of air. These are :

$$IO_4^- \longrightarrow IO_3^- \longrightarrow I^- \xrightarrow[(O_2)]{} I_2 \xrightarrow[(I^-)]{} I_3^-$$

Fig. 2 shows the effect on its absorption spectrum of exposing 10^{-4}M-potassium iodate contained in a closed silica tube to the high-pressure mercury lamp for 1 and for 5 hours. The lowest curve is the absorption curve of the original iodate solution, and the highest is that of pure potassium iodide ($\lambda_{max.} = 224$ mμ, $\varepsilon_{max.} = 12{\cdot}7 \times 10^3$; cf. Scheibe *et al.*, *Z. physikal. Chem.*, 1928, *A*, **139**, 22; 1929, *B*, **5**, 355). On irradiation, the iodate solution develops an absorption band with a maximum close to that in the spectrum of the iodide. The curves show, however, that reduction of iodate to iodide is not the sole reaction, since

FIG. 2. *Optical densities (1 cm.) of:* 10^{-4}M-KIO_3; 10^{-4}M-KI; *and* 10^{-4}M-KIO_3; *exposed to the high-pressure mercury lamp (125 watts, 2 ins.).*

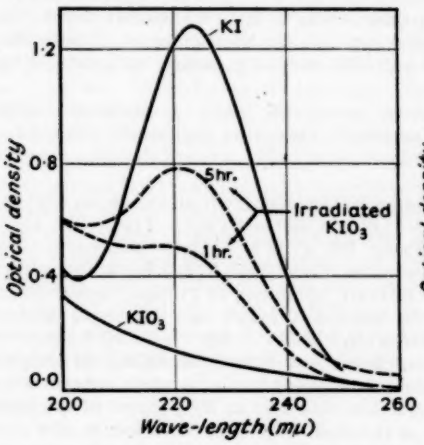
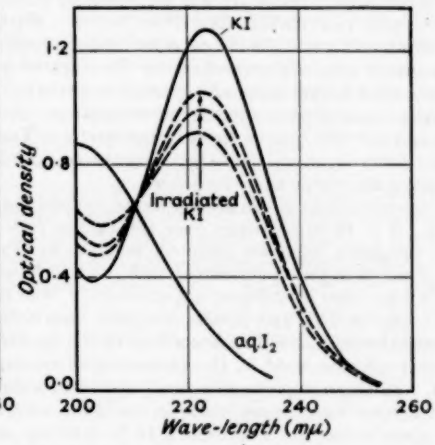


FIG. 3. *Optical densities (1 cm.) of:* 10^{-4}M-KI; 10^{-4}M-KI; *exposed to the high-pressure mercury lamp (125 watts, 5 hours, 2 ins.); and* $0{\cdot}5 \times 10^{-4}$M-I_2 *aq.*



the irradiated iodate solutions have higher absorptions at wave-lengths below 210 mμ than either the pure iodate or the pure iodide. The further reaction responsible for this is the oxidation of iodide ion to iodine, which is known to occur in the presence of air under the influence of short-wave radiation (Oertel, *loc. cit.*).

Fig. 3 shows the absorption curves of potassium iodide solutions, initially 10^{-4}M, before and after exposure in closed silica vessels to the high-pressure mercury lamp in three different experiments. The figure also shows the absorption of an equivalent solution of iodine ($0{\cdot}5 \times 10^{-4}$M-I_2) free from iodide ion; at the lower limit of our working range the absorption is high and still rising ($\varepsilon = 17{\cdot}5 \times 10^3$ at 200 mμ). The five curves in the figure show an isosbestic point at about 210 mμ. The compositions of the irradiated solutions can therefore be expressed in terms of the two components, iodide ion and molecular iodine. This result shows that most of the free iodine in solution is present in the molecular state, and not in combination with iodide, as tri-iodide ion. The conclusion was confirmed by the observation that the absorption of the irradiated solutions was very low over the whole wave-length range from 250 to 400 mμ, whilst the spectral absorption curve of the tri-iodide ion contains two bands in the ultra-violet with very high maxima, one at about 290 mμ ($\varepsilon_{max.} = 40 \times 10^3$), and the other at about 350 mμ ($\varepsilon_{max.} = 26{\cdot}4 \times 10^3$; Awtrey and Connick, *J. Amer. Chem. Soc.*, 1951, **73**, 1842). The absence of tri-iodide ion

in measurable concentration from the irradiated solutions of 10^{-4}M-potassium iodide is due to unfavourable equilibrium conditions. The dissociation constant of the tri-iodide ion-complex obtained by Jones and Kaplan from electrometric measurements is $1{\cdot}4 \times 10^{-3}$ at 25° (*J. Amer. Chem. Soc.*, 1928, **50**, 1845). Calculated from this, the concentration of tri-iodide ion when a solution originally 10^{-4}M in potassium iodide is oxidized to the extent of 20% is about 5×10^{-7}M, which is too low to be observed with certainty by the methods used. When 10^{-3}M-potassium iodide was exposed to the high-pressure mercury lamp under conditions similar to those employed with the more dilute solution, the irradiated solution showed strong absorption at the wave-lengths corresponding to the tri-iodide bands. From the optical density at 290 mμ, and the known extinction coefficient of the tri-iodide ion at this wave-length, the concentration of tri-iodide ion could be obtained; and, from the dissociation constant of the tri-iodide ion, and the known sum of the concentrations of all the iodine species (10^{-3} equiv. per l.), the concentrations of molecular iodine and of iodide ion in the irradiated solution could then be calculated. The latter agreed, within the experimental error, with that obtained from the optical density at 220 mμ, where the absorption is due chiefly to the iodide ion.

Experimental

Sodium metaperiodate was prepared by conventional methods, and was purified before use by several recrystallizations from water. Manganese was a known impurity in the crude material. It could not be detected in the purified salt, and the addition of small quantities of manganese was without effect on the rate of autoreduction of periodate to iodate in light. Iodates and iodides were of " AnalaR " quality.

The spectrophotometric measurements were made at room temperature with a Unicam SP 500 quartz spectrophotometer. The results illustrated graphically are expressed in the form of optical densities as measured, usually in 1-cm. cells; numerical results are quoted as molecular extinction coefficients, ε.

Measurements of the absorption of iodine in aqueous solution free from iodide ion were made with $1{\cdot}5 \times 10^{-4}$M-solutions over the ranges 200—240 and 400—600 mμ. The iodine solution was prepared from an aqueous mixture originally $0{\cdot}5 \times 10^{-4}$M in pure potassium iodate, $2{\cdot}5 \times 10^{-4}$M in pure potassium iodide, and 10^{-2}N in mineral acid (both hydrochloric and sulphuric acids were used in different experiments). The mixture, contained in a closed vessel, was kept for a day at 25°, and it was assumed that both iodate and iodide had then been converted quantitatively into iodine according to the equation $IO_3^- + 5I^- + 6H^+ \longrightarrow 3I_2 + 3H_2O$; the control solution used in the photometric measurements was 10^{-2}N-hydrochloric or -sulphuric acid. In these experiments the iodide and iodate were present in equivalent concentrations. In a further experiment made in the same way, iodate was used in 50% excess of the iodide; the control solution was then a 10^{-2}N-solution of the acid, $0{\cdot}25 \times 10^{-4}$M in iodate (the excess iodate concentration). The curves obtained in these different ways were in fair agreement, and a mean curve was used for the calculation of molecular extinction coefficients. The measurements made in the visible region were in reasonable agreement with the value reported by Awtrey and Connick (*loc. cit.*) at the absorption maximum; we have found no values in the literature with which to compare our measurements in the range of shortest wave-lengths.

In some of the exposures described, the temperature of the irradiated solutions rose appreciably. It was confirmed that the thermal decomposition was negligible compared with the observed photo-chemical effect.

The authors thank Miss M. Bilsbury for the spectrophotometric measurements.

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268. *The Tautomerism of* N*-Hetero-aromatic Amines. Part I.*

By S. J. Angyal and C. L. Angyal.

Data and arguments on the tautomerism of α- and γ-amino-*N*-heterocyclic compounds are critically surveyed, and it is concluded that these compounds exist predominantly in the amino-form. A semi-quantitative method for the estimation of the proportion of the tautomers in equilibrium is proposed which consists in comparing the dissociation constants of the amines with those of suitably methylated derivatives in which tautomerism is not possible. In the cases investigated the ratio of amino- to imino-form was found to be greater than $10^3 : 1$.

Amino-compounds of nitrogen-containing aromatic heterocyclic compounds in which the amino-group is in the α- or the γ-position relative to the ring-nitrogen atom, *e.g.*, 2- and 4-aminopyridine, may exist either as amino-derivatives (*e.g.*, I) or as dihydro-imino-compounds (*e.g.*, II) ("amino-" and "imino-form," respectively). Chichibabin (*Ber.*, 1921, **54**, 814; 1924, **57**, 1168, 2093; 1925, **58**, 1704) used the concept of the imino-form extensively to explain the marked differences in chemical behaviour between the potentially tautomeric amines and those which are not capable of such tautomerism, *e.g.*, 3-aminopyridine (for a tabulation of these differences see Steck and Ewing, *J. Amer. Chem. Soc.*, 1948, **70**, 3397). Since then it has become customary to assign the imino-structure to any heterocyclic amine whose reactions did not correspond with those expected from an aromatic amine. Chichibabin, 25 years ago, had no other means of explaining the different reactivities than by assuming differences in the molecular structures, *i.e.*, tautomerism. Now, however, these differences can be accounted for by the assumption of different *electron distribution* in the molecules, *i.e.*, by mesomerism. Unfortunately no *N*-heterocyclic amine has been isolated in two tautomeric forms, and there exists no method for the estimation of these tautomers. This problem is therefore still controversial, and only recently two groups of investigators arrived at opposing conclusions. Steck and Ewing (*loc. cit.*), from their study of the absorption spectra of amino-pyridines, -quinolines, and -*iso*quinolines, assigned the imino-structure to these compounds. Anderson and Seeger (*ibid.*, 1949, **71**, 340), who also studied the absorption spectra, found no evidence for the presence of imino-forms in solutions of 2- and 4-aminopyridine. It seems therefore that a critical revaluation of the data is warranted.

(I) (Ia) (II) (IIa)

The potentially tautomeric heterocyclic amines are cyclic amidines or vinylogues of amidines. They will therefore show to some extent the properties of both aromatic amines and amidines. As in all amidines, cation formation will occur by addition of a proton to the doubly-bonded nitrogen atom (Branch and Calvin, "The Theory of Organic Chemistry," New York, 1941, p. 196), *i.e.*, to the ring nitrogen in the amino-forms and to the imino-group in the imino-forms. The resulting ion is stabilised by resonance and a second proton is taken up only at a very low pH or not at all. Because of this resonance stabilisation of the cations the potentially tautomeric amines are stronger bases than their isomers (Albert, Goldacre, and Phillips, *J.*, 1948, 2230). The stronger the amidine character of the amine the greater is this exaltation of the basic strength.

In many cases suggestions that the amines have the imino-structure are based solely on the products of chemical reactions. Such evidence is valueless because the tautomeric form responsible for the reaction may be present in only a minute amount and be formed as the reaction proceeds. Non-occurrence of a reaction expected from one tautomeric form is, however, admissible evidence: it may prove that one of the forms is totally absent. Most of the evidence quoted in favour of the imino-form is of such a nature. The

best evidence is obtained, however, by studying the physical properties of the tautomers in equilibrium.

The Case for the Imino-forms.—(1) *Alkylation.* In the first paper (Chichibabin, Konowalowa, and Konowalowa, *Ber.*, 1921, **54**, 814) of a series entitled "The Tautomerism of 2-Aminopyridine," Chichibabin found that methyl iodide reacted with the ring-nitrogen atom of bases such as 2- and 4-aminopyridine. He did not claim this as evidence that the bases exist in the imino-form (as later authors did, cf. Steck and Ewing, *loc. cit.*) but only stated that they react in this form. However, from our knowledge that amidines are methylated on their doubly-bound nitrogen atom (Pyman, *J.*, 1923, 3359) and from a consideration of the electron distribution in these compounds (cf. dipole moments, below) it is now obvious that the ring-nitrogen atom will be methylated in the *amino-*, not in the imino-, form. It has been shown (Angyal, *Austral. J. Sci. Res.*, in the press) that acylating agents also attack the ring-nitrogen atom. Nevertheless this argument for the imino-form is still sometimes used: *e.g.*, Albert and Ritchie (*J.*, 1943, 458), who found that the ring-nitrogen atom is methylated by methyl iodide in 5-aminoacridine whereas it does not react in the other aminoacridines, state that "the usually unreactive tertiary ring nitrogen is reacting as a secondary amine because of tautomerism." The tautomeric imino-form would, undoubtedly, be methylated on the imino-group. The enhanced nucleophilic reactivity of the ring-nitrogen atom is probably due to the strong resonance in 5-amino-acridine which causes high electron density on the ring-nitrogen atom.

Equally unconvincing is the assignment of the imino-structure to 9-amino-phenanthridine (Morgan and Walls, *J.*, 1932, 2227) on the basis of its acetylation which appears to give a ring-acetyl derivative.

(2) *Diazotisation.* The potentially tautomeric *N*-hetero-aromatic amines are not diazotised by nitrous acid in dilute solutions of acids (Marckwald, *Ber.*, 1894, **27**, 1317; Albert and Ritchie, *loc. cit.*; Morgan and Walls, *loc. cit.*) but only in concentrated acid solution (Königs, Kinne, and Weiss, *Ber.*, 1924, **57**, 1172). Diazonium salts, however, cannot be obtained but the corresponding hydroxy-compounds are formed. These facts have sometimes been used as arguments for the imino-form but can be explained without invoking it. Resonance (I $\longleftrightarrow$ I*a*) causes low electron density on the amino-nitrogen atom, insufficient for reaction with the but weakly electrophilic dinitrogen trioxide molecule (Ingold, Hughes, and Ridd, *Nature*, 1950, **166**, 642) In concentrated acid solutions, however, the strongly electrophilic nitrosonium ion is present and will react. The case is analogous to that of polynitro-substituted anilines. The instability of the diazonium salts is similarly explained: aromatic diazonium salts are stabilised by resonance involving electrons from the aromatic ring (Dewar, "The Electronic Theory of Organic Chemistry," Oxford Univ. Press, 1949, p. 182). In the *N*-hetero-aromatic series the strong electron attraction of the ring-nitrogen atom prevents this resonance and therefore the diazonium compounds are as unstable as the aliphatic ones.

(3) *Hydrolysis.* Many potentially tautomeric amines are hydrolysed by acid or alkali to the corresponding hydroxy-compounds; this has often been taken as an indication for their existence in the imino-form (Morgan and Walls, *loc. cit.*; Marshall and Walker, *J.*, 1951, 1004). It is true that compounds which definitely have the imino-structure, such as 1 : 4-dihydro-4-imino-1-methylpyridine, are readily hydrolysed by alkalis. However, 5-amino-, 5-methylamino-, and 5-dimethylamino-acridine are all hydrolysed to acridone, the last—which *cannot* exist in the imino-form—the most easily (Albert and Ritchie, *loc. cit.*).

The ease of hydrolysis probably indicates low electron density on the carbon atom to which the amino-group is attached rather than the presence of an imino-form. This is borne out by a comparison of 4-amino-quinoline, -cinnoline, and -quinazoline (Keneford, Morley, Simpson, and Wright, *J.*, 1950, 1104); only the last-named compound is hydrolysed by acids and in this compound the electron density on $C_{(4)}$ is particularly low.

Exactly the opposite argument was used by Goodall and Kermack (*J.*, 1936, 1546). Observing that 5-aminoacridines containing disubstituted amino-groups are more readily hydrolysed by acids to acridones than are those with only one *N*-substituent, they concluded that the compounds with tertiary amino-groups are in the amino-forms but those with

secondary amino-groups exist in the imino-form. There seems to be no logical basis for this argument. 5-Dimethylaminoacridine is also hydrolysed by acids (Albert and Ritchie, *loc. cit.*). The most probable explanation is steric hindrance of resonance; the disubstituted amino-group cannot become coplanar with the aromatic rings and therefore the resonance stabilisation in this compound will be less than in the mono-substituted derivatives. The reduced resonance is clearly visible in the smaller exaltation of the basic strength: 5-amino-, -methylamino-, and -dimethylamino-acridine have pK_a 9·45, 9·77, and 7·53, respectively, whereas 2-amino- and 2-dimethylamino-acridine have practically identical pK_a values, there being no steric hindrance (Albert and Goldacre, *J.*, 1946, 706; Albert, "The Acridines," Edward Arnold & Co., London, 1951, p. 122).

(4) *Schiff's bases.* Some *N*-hetero-aromatic amines do not condense with aldehydes. Thus 5-aminoacridine does not react with benzaldehyde or salicylaldehyde (Albert and Ritchie, *loc. cit.*), and 4-aminopyrimidines do not react with sugars (Baddiley, Lythgoe, and Todd, *J.*, 1943, 571). In both cases the conclusion was drawn that the amines behave like imino-compounds. The more probable explanation again involves the low electron density on these amino-nitrogen atoms which will prevent nucleophilic addition to the carbonyl carbon atom of the aldehyde. Tables of calculated electron densities (Longuet-Higgins and Coulson, *J.*, 1949, 975: Pullman, *Rev. Sci.*, 1948, **86**, 219) show that at $C_{(4)}$ in pyrimidine and at $C_{(5)}$ in acridine the electron density is particularly low; this effect would be transmitted to an attached amino-group. 2-Aminoacridine occupies an intermediate position: it does not react with benzaldehyde but condenses with the more reactive salicylaldehyde (Albert and Ritchie, *loc. cit.*).

The Case for the Amino-forms.—(1) *Resonance energy.* The energetics of the amino–imino tautomeric system have apparently not been considered. The amino-forms have a fully aromatic structure and benefit by the aromatic resonance energy; the imino-forms, however, have a quinonoid structure in which some of the aromatic resonance energy has been lost. In consequence one would expect the amino-form to have the lower energy, and therefore to be more stable, in all the hetero-aromatic amines (unless substituents which have a strong influence on electron densities interfere).

Also, the analogy with the corresponding hydroxy-derivatives is often emphasised. For these compounds the pyridone, quinolone, acridone, etc., structures are well established (see, *e.g.*, Mosher in Elderfield's "Heterocyclic Compounds," Wiley, New York, 1950, Vol I, p. 435). The two classes of compounds, however, are not analogous. Branch and Calvin (*op. cit.*, p. 289) have calculated from Pauling's bond-energy values that in the amide–imidol tautomeric system, ·NH·C:O ⇌ ·N:C·OH, the former tautomer is the more stable to the extent of about 10 kcal./mole. This gain in bond energy may compensate for the loss of resonance energy in the tautomerisation from hydroxypyridine to pyridone. But in the amino-compounds the tautomeric system is that of amidines, ·NH·C:N· ⇌ ·N:C·NH· in which there is no change in bond energies; there is nothing therefore to compensate for the loss of resonance energy.

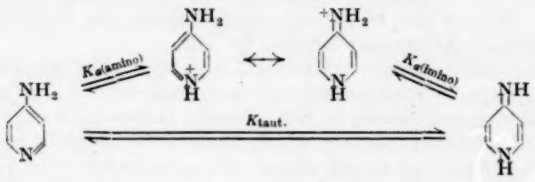
(2) *Dipole moments.* The evidence based on dipole moments is not conclusive. Leis and Curran (*J. Amer. Chem. Soc.*, 1945, **67**, 79) have reported that the dipole moment of 4-aminopyridine is somewhat larger than that calculated by combining the values for pyridine and aniline. This is concordant with the amino-form (I) with a resonance contribution from (I*a*). According to these authors the imino-form (II) cannot be present in any significant amount since it would have a very low moment. It seemed to us, however, that the structure of the imino-form would have a very considerable contribution from (II*a*), owing to its strong tendency to revert to the aromatic system, and therefore would be strongly rather than weakly polar. Accordingly we tried to measure the moment of 1:2-dihydro-4-imino-1-methylpyridine—a compound which can have only the imino-structure—but were prevented by its low solubility in benzene and dioxan. However, the measurements were carried out in the quinoline series: 4-aminoquinoline was found to have a moment of 4·4 D—the same as 4-aminopyridine—and 1:4-dihydro-4-imino-1-methyl quinoline a moment of 5·1 D. A high dipole moment is, therefore, no evidence for the amino-form.

(3) *Absorption spectra.* Conclusions have been often drawn on the tautomerism of

N-heterocyclic amines from the study of absorption spectra. These conclusions are unreliable, however, unless information is available about the bands occurring in the spectra of both the amino- and the imino-forms.* Since replacement of a hydrogen atom by a methyl group causes only minor changes in the spectrum, such information can be obtained from the spectra of methylated derivatives in which tautomerism has been eliminated. By this method, Anderson and Seeger (*loc. cit.*) have shown that the characteristic band of the imino-form does not appear in the spectra of 2- and 4-aminopyridines and consequently the imino-form, if it exists at all, can be present in very small proportion only.

(4) In two cases, those of melamine (Knaggs and Lonsdale, *Proc. Roy. Soc.*, 1940, **177**, A, 140; Hughes, *J. Amer. Chem. Soc.*, 1941, **63**, 1737) and of 4-amino-2 : 6-dichloropyrimidine (Clews and Cochran, *Acta Cryst.*, 1950, **3**, 76), the amino-structure was proved by *X*-ray analysis.

From this survey it appears that the amino-form is the more stable and therefore predominates in the *N*-hetero-aromatic amines. But all the above-mentioned information on the tautomeric equilibrium is only qualitative. Yet there exists a simple method, based on the determination of the basic strength, which yields quantitative values for the tautomeric equilibrium constant, with a certain approximation (cf. Branch and Calvin, *op. cit.*, p. 301). Since both the amino- and the imino-form give the same mesomeric cation by the addition of a proton, the following equilibria coexist:



in this scheme $K_{a(\text{amino})}$ and $K_{a(\text{imino})}$ are the acid dissociation constants of the cation as the conjugate acid of the amino- and the imino-form, respectively, and $K_{\text{taut.}}$ is the tautomeric equilibrium constant. Since

$$K_{a(\text{amino})} = [\text{amino}][H^+]/[\text{cation}]$$

and

$$K_{(a)\text{imino}} = [\text{imino}][H^+]/[\text{cation}]$$

it follows that

$$K_{\text{taut.}} = [\text{amino}]/[\text{imino}] = K_{a(\text{amino})}/K_{a(\text{imino})} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

i.e., the tautomeric equilibrium constant can be calculated from the two dissociation constants. This relation is generally valid for all tautomeric equilibria where the two tautomers give the same cation (or anion); in a qualitative sense it requires the less prevalent tautomer to be the stronger base (or acid). Many examples could be quoted; thus imino-esters are stronger bases than amides; *iso*ureas and *iso*thioureas are stronger bases than ureas and thioureas, respectively; the nitroalkanes are weaker acids than their *aci*-forms, and simple enols are stronger acids than the corresponding ketones [although equation (1) indicates that the unknown *cyclo*hexa-2 : 4-dienone, the ketonic tautomer of phenol, must be a stronger acid than phenol].

Application of this simple relation is restricted by the difficulty of determining the dissociation constants of both tautomeric forms. Apparently this has been achieved

* A recent example of an unjustified conclusion from spectra is the assignment of the imino-structure to 4-aminoquinoline and 4-aminocinnoline (Hearn, Morton, and Simpson, *J.*, 1951, 3318) on the basis of the resemblance of their spectra to those of 4-quinolone and 4-cinnolone, respectively. There is no reason, however, why the *O*- and the *N*-derivatives should absorb at the same wave-length. In fact, comparison of the ultra-violet spectra of 2- and 4-ethoxypyridine and 2- and 4-pyridone on the one hand (Specker and Gawrosch, *Ber.*, 1942, **75**, 1338), and the corresponding aminopyridines and dihydroimino-*N*-methylpyridines on the other (Anderson and Seeger, *loc. cit.*) shows that in all cases the *N*-derivatives absorb at a longer wave-length than the analogous *O*-derivatives.

only in the case of the nitroalkanes (Turnbull and Maron, *J. Amer. Chem. Soc.*, 1943, **65**, 212) where the tautomeric equilibrium constants have been calculated according to equation (1).

Since the tautomeric forms of the heterocyclic amines are not known, their ionisation constants cannot be directly determined. As an approximation, however, the corresponding constants of their known methylated derivatives can be substituted. The error introduced is not large since methyl substitution usually increases pK_a by about 0·2 unit only (Hall and Sprinkle, *ibid.*, 1932, **54**, 3469; see also Albert and Goldacre, *loc. cit.*, 1946). Thus the dissociation constant of the dihydro-imino-*N*-methyl compound can be substituted for $K_{a(\text{imino})}$; and, since—as the results show—the amino-form predominates considerably, the experimentally determined constant of the heterocyclic amine, K_a, will be nearly identical with, and can be used instead of, $K_{a(\text{amino})}$. In other cases, where the equilibrium is not one-sided to such an extent, it will be necessary to substitute the dissociation constant of the corresponding dimethylamino-compound for $K_{a(\text{amino})}$.

This method has apparently been applied only once to tautomeric equilibria: by Tucker and Irvin (*ibid.*, 1951, **73**, 1923) to 4-quinolone. Independently of the American authors we have investigated (C. L. Angyal, Thesis, Sydney, 1951) some heterocyclic amines; our results, together with published data on melamine, are shown in the Table.

	pK_a	$pK_{a(\text{Me})}$ *	$K_{\text{taut.}}$ †	ΔF (kcal./mole)
2-Aminopyridine	6·86 ‡	12·20 §	2×10^6	7·3
4-Aminopyridine	9·17 ‡	12·5 §	2×10^3	4·5
4-Aminoquinoline	9·17 ‡	12·4 §	2×10^3	4·5
2-Aminothiazole	5·39 ‡	9·65 §	2×10^4	6·0
Melamine (2 : 4 : 6-triamino-1 : 3 : 5-triazine)	5·16 ‡	10·54 ‖	2×10^5	7·3

* pK_a of the corresponding dihydro-imino-*N*-methyl compound.
† Calculated from equation (1), with K_a instead of $K_{a(\text{amino})}$, and $K_{a(\text{Me})}$ instead of $K_{a(\text{imino})}$.
‡ Albert, Goldacre, and Phillips, *loc. cit.* § Present work.
‖ Value for ethyl*iso*melamine, Dudley, *J. Amer. Chem. Soc.*, 1951, **73**, 3007.

The imino-compounds derived from the amino-pyridines and -quinoline show a basic strength typical of amidines (*e.g.*, acetamidine, pK_a 12·52; Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1162), and 1 : 4-dihydro-2-imino-3-methylthiazole has a strength comparable to that of *S*-methyl*iso*thiourea (pK_a 9·83, Albert, Goldacre, and Phillips, *loc. cit.*). The imino-forms of other heterocyclic amines would presumably show the same non-aromatic basic strength, and since all the heterocyclic amines so far measured have considerably lower pK_a's, they probably all exist in the amino-form.

The last column of the Table gives the difference of the free energies of the tautomers, calculated from the equation $\Delta F = -RT \ln K_{\text{taut.}}$. Since the bond energies of the tautomers are equal, this difference in the free energies is mainly due to resonance and is therefore a measure of the loss of aromatic resonance energy in the change from the amino- to the imino-form.

The above conclusions are valid only for the dilute aqueous solutions in which the pK_a values were determined; but the ΔF values are sufficiently large to make it unlikely that the position of the equilibrium would be reversed by a change of solvent. It is worth mentioning that the absorption spectra of 2- and 4-aminopyridine are the same in water and in ether (Anderson and Seeger, *loc. cit.*).

Experimental

Materials.—4-Aminopyridine and 4-aminoquinoline, as well as their methiodides, were prepared by Mr. N. K. Matheson according to published methods (Chichibabin and Ossetrova, *Ber.*, 1925, **58**, 1709; Claus and Frobenius, *J. pr. Chem.*, 1897, **56**, 184). The methiodide, m. p. 149°, of 2-aminopyridine was made according to Chichibabin, Konowalowa, and Konowalowa (*loc. cit.*). The methiodide of 2-aminothiazole was prepared by boiling a solution of the amine (5 g.) in anhydrous ethanol (5 c.c.) with methyl iodide (7 g.) for 10 minutes and crystallising the yellow precipitate from anhydrous ethanol. It melted at 174°; Nef, who prepared it in a sealed tube at 130°, reported m. p. 175° (*Annalen*, 1891, **265**, 112).

Ionisation Constants.—Approx. 0·01M-aqueous solutions of the hydriodides were titrated

potentiometrically at 21° with 0·1N-potassium hydroxide. The pH values were determined with a Leeds and Northrup Universal pH Potentiometer Assembly (No. 7663-A-1), adjusted to pH 9·16 by comparison with a M/20-borax buffer. The solutions were made in carbon dioxide-free water and were titrated in a stream of nitrogen. The pK_a values were calculated according to the equation, $pK_a = pH - \log\{([B] - [OH^-])/([BH^+] + [OH^-])\}$, where [B] and $[BH^+]$ are the calculated concentrations of the base and its conjugate acid, respectively, corrected for the dilution caused by addition of alkali but not for the activity coefficients or for the potassium-ion error. Above pH 12 the values were not readily reproducible and the error in pK_a may there be as high as 0·2 unit.

Dipole Moments.—Details of procedure and calculations were as recorded by Calderbank and Le Fèvre (*J.*, 1948, 1949; cf. also Le Fèvre, *Trans. Faraday Soc.*, 1950, **46**, 1). 1 : 4-Dihydro-4-imino-1-methylquinoline is described as an oil (Claus and Frobenius, *loc. cit.*) but we found that it crystallised on evaporation of its solution in benzene. Because of its extreme sensitivity to oxygen, carbon dioxide, and water, however, it seemed unsuitable for purification, analysis, and weighing. Instead, the base was liberated from a solution of its hydriodide by concentrated sodium hydroxide solution and extracted by chloroform, and the extract dried (Na_2SO_4) and evaporated *in vacuo*. Dry benzene was then added, the whole was evaporated several times to remove all water and chloroform, and the benzene solution was filtered and used directly for dipole moment measurements. The concentration was determined by acidimetric titration (phenolphthalein) of an aliquot. (The base, as it separates from water, is not soluble in benzene probably because of hydrate formation.)

The measurements are tabulated under the usual headings (Calderbank and Le Fèvre, *loc. cit.*).

$10^5 w_1$	ε	d_4	$a\varepsilon_2$	β
4-Aminoquinoline in dioxan at 25°				
0	2·2192	1·0303	—	—
457	2·2990	1·0313	17·46	0·2124
684	2·3342	1·0317	16·81	0·1986
1010	2·3955	1·0321	17·46	0·1731
whence $a\varepsilon_2 = 17·24$ (mean); $\beta = 0·195$ (mean).				

$10^5 w_1$	ε	d_4	$a\varepsilon_2$	β
1 : 4-*Dihydro-4-imino-1-methylquinoline in benzene at* 30°				
0	2·2628	0·86718	—	—
671	2·3835	0·86901	18·00	0·3179
1017	2·4415	0·86988	17·57	0·3062
1261	2·4920	0·87061	18·18	0·3137
whence $a\varepsilon_2 = 17·92$ (mean); $\beta = 0·313$ (mean).				

	M	P_T (c.c.)	$[R_L]_D$	μ (D)
4-Aminoquinoline	144·2	439·4	46·6	4·38
1 : 4-Dihydro-4-imino-1-methylquinoline	158·2	577·0	51·2	5·11

The authors are indebted to Mr. N. K. Matheson for preparative assistance, and to Professor A. Albert for a helpful discussion.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, December 3rd*, 1951.]

269. *The Molecular Structure of Pyrrole and Some of its Simple Derivatives, from Electric Dipole Moment Measurements.*

By Helmer Kofod, L. E. Sutton, and (in part) J. Jackson.

Seventeen pyrrole derivatives have been investigated. The electric dipole moments are consistent with the conclusions about ring structure from other physical methods. They indicate that the extra-annular nitrogen valency is not more than 7° out of the symmetry axis of the ring. The direction of the π-electron moment of pyrrole has been determined. It agrees with deductions from organic chemical evidence, and from theoretical considerations, in having its positive pole towards the nitrogen and its negative one towards the remainder of the ring.

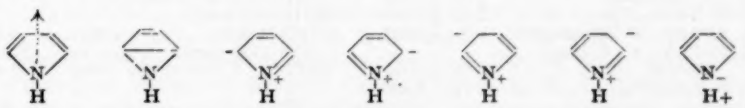
Resonance phenomena and the steric inhibition thereof have been studied in a series of *N*-phenylpyrrole derivatives. The π-moment due to interannular conjugation has been estimated to be *ca.* 0·5 D, antiparallel to the main moment of phenylpyrrole.

A series of indole derivatives measured by Janetsky and Lebret has been included in the discussion. These and all the reported pyrrole derivatives fit into a general pattern.

Electronic Structure and Geometry of the Pyrrole Ring: Previous Information from Other Methods.

Pyrrole has benzene-like aromatic character. The language used to account for this has changed from time to time, but the essential idea remains the same. The aromaticity is now generally attributed to a sextet of unlocalized π-electrons, the nitrogen providing by its lone pair the two electrons necessary to complete the sextet. According to the molecular-orbital treatment (Coulson and Longuet-Higgins, *Trans. Faraday Soc.*, 1947, **43**, 87) the delocalization of the lone pair is so effective as to leave the nitrogen with a formal positive charge in spite of the fact that its electronegativity is higher than that of carbon. A corresponding negative charge is distributed over the carbon atoms in the ring. The pyrrole ring will therefore possess an electric dipole moment due to the π-electron distribution (often referred to as the π-moment), apart from the resultant of the σ-bond moments.

In the terms of the valence-bond method the electron distribution may be described by the resonating structures shown below. From the formally charged structures (iii)—(vii) contributing to the resonance hybrid it is to be expected that the π-moment will have its negative pole uppermost in the formulæ written as below. Further, since (iii) and (iv) have the same weight, likewise (v) and (vi), the π-moment should be parallel to the symmetry axis which the ring itself may be presumed to have.



By an electron-diffraction examination, Pauling and Schomaker (*J. Amer. Chem. Soc.*, 1939, **61**, 1778) found dimensions for pyrrole which agreed with the ring's being planar. The bonds 2–3 and 4–5 are slightly shorter, 1·35 Å, than the other bonds, 1·42 Å, showing that the classical structure (i) contributes most to the hybrid. No one of the intra-annular valency angles deviates from 108° by more than the experimental error. It is therefore sufficient for the present purpose to regard the pyrrole ring as a coplanar regular pentagon having a side of length 1·4 Å.

The electron-diffraction method cannot place the hydrogen atoms in pyrrole. Garach

and Lecomte (*Bull. Soc. chim.*, 1946, 415; *Compt. rend.*, 1946, **222**, 74) report that the infra-red absorption spectrum of pyrrole is readily explained by a model having all bonds, including the C–H bonds, coplanar; but there seems still to be some doubt about the direction of the N–H bond relatively to the ring plane. The above authors conclude that this bond is inclined to the ring plane, but others differ: *e.g.*, Lord and Miller (*J. Chem. Physics*, 1942, **10**, 339) conclude that the Raman and infra-red spectra strongly support a coplanar structure, although a non-coplanar one is not definitely ruled out. If, as is supposed in the theoretical treatment (Coulson and Longuet-Higgins, *loc. cit.*), the three σ-bonds of the nitrogen are formed by hybridization of one *s*- and two *p*-orbitals, it would be expected that they would be coplanar. The establishment of this point would therefore be a useful verification of the said treatment.

The present investigation fails to provide conclusive evidence as to the direction of the N–H bond; but it gives limits to the degree of non-coplanarity.

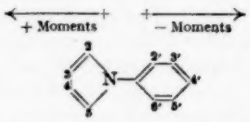
Calculation of the Electric Dipole Moment of Pyrrole.—Neither the moment due to the electrons in the σ-bonds nor that due to those in the π-bonds of pyrrole can be accurately calculated *a priori*, but a rough estimate may be attempted. Taking values of 0·4 D for H–C, 1·3 D for H–N, and 0·5 D for C–N (cf., *e.g.*, Hill and Sutton, *J.*, 1949, 746; Everard and Sutton, *J.*, 1949, 2320) * and assuming the geometry of pyrrole to be as outlined above, we get a resulting σ-moment of about +0·4 D.† The π-moment may be approximately calculated from the π-electron densities obtained by Coulson and Longuet-Higgins (*loc. cit.*). The result is +1·97 D. However, owing to certain approximations, such molecular-orbital treatments are prone to exaggerate the π-electron moment (see Orgel, Cottrell, Dick, and Sutton, *Trans. Faraday Soc.*, 1951, **47**, 113 ‡). Pauling and Schomaker (*loc. cit.*) derived an experimental value of the π-moment and used this to assess the importance of contributions by structures (iii)—(vi). They found that the results agreed quite reasonably with those obtained from the bond lengths. A σ-moment of +0·4 D being taken, it follows that if the observed moment, 1·80 D, is positive, the π-moment is +1·40 D. Pauling and Schomaker (*loc. cit.*) give a value, similarly derived, of 1·5 D.

TABLE 1. *Electric dipole moments of pyrrole derivatives in benzene solution at 25°.*
(*Debye units.*)

Pyrroles.

(I) Unsubstituted	1·80 ± 0·01	(IV) 1 : 2 : 5-Trimethyl	2·07 ± 0·01
(II) 1-Methyl	1·92 ± 0·02	(V) 3 : 4-Di-iodo-2 : 5-dimethyl	4·00 ± 0·01
(III) 2 : 5-Dimethyl	2·08 ± 0·03	(VI) 2 : 3 : 4 : 5-Tetraiodo	2·52 ± 0·04

1-Phenylpyrroles.



(VII) Unsubstituted	1·32 ± 0·04	(XII) 2 : 5 : 4′-Trimethyl	2·34 ± 0·02
(VIII) 2 : 5-Dimethyl	2·00 ± 0·04	(XIII) 4′-Chloro	*ca.* 0·03
(IX) 2 : 5 : 2′ : 5′-Tetramethyl	2·07 ± 0·02	(XIV) 4′-Chloro-2 : 5-dimethyl	0·50 ± 0·04
(X) 2 : 5 : 2′ : 4′ : 6′-Pentamethyl	2·06 ± 0·04	(XV) 4′-Bromo-2 : 5-dimethyl	0·54 ± 0·03
(XI) 4′-Methyl	1·79 ± 0·04	(XVI) 2 : 5-Dimethyl-4′-nitro	2·48 ± 0·02

p-Di-1-pyrrylbenzene.

(XVII) *p*-Bis-(2 : 5-dimethyl-1-pyrryl)benzene ..... 0·77 ± 0·03

* The convention used here is that the right-hand atom bears the negative dipolar charge.

† A plus sign denotes a moment parallel to the symmetry axis of pyrrole and with its negative end upwards in the formulæ written as in (i)—(vii), whereas a minus sign shows a moment in the opposite direction.

‡ These authors did not calculate an independent value for the moment of pyrrole but used the observed value to derive a parameter for nitrogen.

Discussion

(*A*) *The Monocylic Compounds* (I) —(VI) (*Table* 1).—Two of the compounds in Table 1 were measured in 1933 by one of us (J. J.), namely, pyrrole (I) and 1-methylpyrole (II), and the results were briefly reported (Sutton, *Trans. Faraday Soc.*, 1934, **30**, 789). The moments have been recalculated from the observations by the method of Halverstadt and Kumler (*J. Amer. Chem. Soc.*, 1942, **64**, 2988), which has been used throughout this paper. No other records of the moment of 1-methylpyrrole have been found. Other values reported for pyrrole are 1·83 at 20° (Cowley and Partington, *J.*, 1933, 1259); 1·80 at 20° (Robles, *Rec. Trav. chim.*, 1939, **58**, 111); 2·2—2·0 at 20°, 1·8 at 22°, and 1·7 at 23° (Hückel, Datow, and Simmersbach, *Z. physikal. Chem.*, 1940, *A*, **186**, 166). The figures from the last reference are each based on only one solution and are hence deemed less reliable.

For considering the moments of many of the other compounds the group moment of $Me-C_{ar.}$ is needed, *i.e.*, the extra moment produced when a hydrogen atom attached to carbon in the pyrrole ring is replaced by a methyl group. In view of the similarity of the aromatic systems of pyrrole and benzene, we shall assume this group moment to be equal in magnitude and direction to the moment of toluene 0·35 D, *i.e.*, $\overset{+}{C}H_3-\overset{-}{C}_{ar.}$. Some support for this assumption comes from the moments of alkylindoles. Indole is assumed to contain an undistorted regular pyrrole ring and the entire molecule is taken as coplanar. From the practically identical experimental values 2·11 and 2·08 found for indole and 3-methylindole (Janetzky and Lebret, *Rec. Trav. chim.*, 1944, **63**, 123), it follows that either the $Me-C_{ar.}$ moment is vanishingly small, which is very unlikely, or it is oriented almost orthogonally to the main moment of indole. This means, however, that in 2-methylindole the main moment and the $Me-C_{ar.}$ moment are practically parallel. We should therefore be able to get a reliable value for the latter as the difference between the moment of 2-methylindole, 2·47 (*loc. cit.*), and that of indole 2·11, *i.e.*, 0·36. Hence the value chosen, 0·35 D, seems to be reasonable.

The moment calculated for 2 : 5-dimethylpyrrole (III) on the assumptions already given and the moment of pyrrole being taken as 1·80 D, is +2·02 D. The observed moment is 2·08 ± 0·03 D. This agreement confirms that the pyrrole moment is positive. The fact that the agreement is so good furthermore suggests that the H–N bond is at least roughly coplanar with the ring, as the calculated moment of any reasonable non-coplanar molecule would be *lower* than 2·02 D.

Similarly, the moment of 1 : 2 : 5-trimethylpyrrole (IV) derived from the value 1·92 D observed for 1-methylpyrrole (II) is 2·14 D (cf. 2·07 D observed).

The reasonably good vector additivity found for these compounds is obviously no rigorous proof of coplanarity, for the contribution of a substituent moment of only 0·35 D to the final moment is too small compared with the probable error in the values (0·02—0·05 D). It was therefore hoped that a clearer answer might be obtained by using a substituent with a somewhat higher moment, and so the iodo-derivatives (V) and (VI) were used. In order to be able to compare these with the parent compounds (III) and (I), the difference of the moments of $C_{ar.}-I$ and $H-C_{ar.}$ is needed. It will be taken as the moment of iodobenzene, thus making an empirical allowance for the π-moment in *C*-iodopyrrole by assuming it to be equal to the one in iodobenzene. The value taken is 1·42 D (Mr. M. J. Saxby, private communication); earlier values varying from 1·25 to 1·38 D are given by Walden and Werner (*Z. physikal. Chem.*, 1929, *B*, **2**, 10), Bergmann *et al.* (*ibid.*, 1930, *B*, **10**, 106), and Tiganik (*ibid.*, 1931, *B*, **13**, 425). Assuming the simple ring geometry already described, and making no allowance for the various induced moments, we obtain 4·38 D for 3 : 4-di-iodo-2 : 5-dimethylpyrrole. When allowance is made for induced moments ($C_{ar.}-I$ moment on iodine and pyrrole moment on iodine) by Hampson and Weissberger's method (*J.*, 1936, 393) we obtain 4·24 D. The agreement with the observed value 4·00 D is only fair and may possibly indicate some non-coplanarity of the N–H bond; but the corrections for induced moments are not very precise. For 2 : 3 : 4 : 5-tetraiodopyrrole (VI), a similar basis being used and without corrections for induced moments, a value of 3·22 D is obtained. When corrected, this becomes 2·48 D, which agrees well with the observed value of 2·52 D; but in view of the previous result we regard this agreement as

somewhat fortuitous. These results for the iodo-derivatives obviously confirm the previous conclusions about the direction of the pyrrole moment but do not provide decisive evidence for a coplanar N–H bond.

From the moments of pyrrole (1·80) and of 1-methylpyrrole (1·92) it appears that the effective moment of Me–N exceeds that of H–N by 0·12 D, whereas the σ-moment of Me–N is *lower* than that of H–N by about 0·5 D (H–N 1·3 against Me–N 0·85 D from ammonia and trimethylamine, respectively). Hence we have to explain an extra moment of +0·6 superimposed upon the normal σ-moment in Me–N. As for the toluene moment, we can put forward several hypotheses all having the feature in common that they are formal "explanations" in different languages expressing our ignorance rather than our knowledge (see, *e.g.*, Hurdis and Smyth, *J. Amer. Chem. Soc.*, 1943, **65**, 89; Baker *J.*, 1939, 1150; Le Fèvre, Le Fèvre, and Robertson, *J.*, 1935, 480). Some explanations can, however, be ruled out.

It is, for instance, unlikely to be due to solvent effect, which should be much the same in pyrrole and in 1-methylpyrrole; nor is it due to association. Hydrogen bonding, giving head-to-head association between a pair of pyrrole molecules, would admittedly reduce the observed moment of pyrrole and could thus account for the discrepancy. But, although the relatively high boiling point is some indication of this, the total polarization of pyrrole in benzene solution varies very little with concentration and in any case no more than does that of 1-methylpyrrole (see p. 1475).

The apparent extra moment of Me–N in methylpyrrole may be explained by the greater electronegativity of the nitrogen atom in pyrrole than in the aliphatic compounds, owing to the formal positive charge given by π-electron redistribution. The effect of the increased electronegativity would be more marked in 1-methylpyrrole than in pyrrole because of the greater polarizability of the methyl group.

The anomaly may also originate from the different hybridization of the nitrogen atom in the aliphatic and in the cyclic state. Further light might be thrown upon this problem by the dipole moments of other *N*-alkyl-pyrroles.

(*B*) *Collinearity of Ring Axes in the* 1-*Phenylpyrroles* (VII)—(XVI).—These compounds were investigated with the aim of studying the interaction between the two aromatic rings, and the steric and electronic influence on this interaction of substitutents introduced in either ring.

In 1-phenylpyrrole itself a certain degree of interannular conjugation is to be expected. It may be visualized from a series of resonating structures having a positive charge on the nitrogen atom, a negative one on the benzene ring (*o*- or *p*-position), and an interannular double bond.

The resonance energy in 1-phenylpyrrole due to the interannular conjugation has been estimated by Pauling and Schomaker (*loc. cit.*) from combustion data as 6 kcal./mol. In diphenyl the conjugation energy is 8 kcal./mol. (Pauling and Sherman, *J. Chem. Physics*, 1933, **1**, 606, 679). It is reasonable that the interannular conjugation energy is lower in 1-phenylpyrrole, since the nitrogen atom is already involved in *intra*annular conjugation.

In order that the conjugation energy may be as large as possible, the two rings will tend to be more or less coplanar. Bastiansen (*Acta Chim. Scand.*, 1949, **3**, 408) concludes from an electron-diffraction examination that, in the vapour state, diphenyl is linear with the two ring planes mutually twisted 45° ± 10° round the interannular bond. Neither the coplanar nor the orthogonal configuration is satisfactory. In the crystalline state, on the other hand, diphenyl is found to be linear and coplanar (Dhar, *Indian J. Physics*, 1932, **7**, 43). The structure of the molecule will probably not differ very much in the vapour state and in dilute solutions. The angle 45° suggested agrees in this case with the conclusions from a scale diagram (Fig. 1). There is an appreciable steric interference between the hydrogen atoms in *o*-positions to the interannular bond. In *N*-phenylpyrrole (Fig. 2), however, the steric interference is considerably less (0·3 Å overlap compared with 0·6 Å in diphenyl) because, although the Ph–N bond is shorter than the Ph–Ph bond, the pentagonal pyrrole ring increases the clearance of the *o*-hydrogen atoms. This molecule may therefore well be coplanar or nearly so in spite of the interannular resonance energy being smaller than in the non-coplanar diphenyl.

The interannular conjugation will manifest itself in an extra π-moment probably of negative sign (negative pole towards phenyl nucleus). This direction will be shown to be correct, and the magnitude estimated by using the device of steric inhibition of resonance (Section C). To effect this demonstration properly, however, we need information about the inclination of the N–Ph link relatively to the pyrrole ring axis both in the conjugated (VII, XI, XIII) and in the non-conjugated 1-phenylpyrroles (VIII, IX, X, XII, XIV, XV, XVI). Whereas the former are *a priori* almost certainly axially collinear, it is less certain that the latter are. The facts are the following.

The observed moment of 1-phenylpyrrole (VII) is 1·32 D. Adding the moment of toluene 0·35 D, we get 1·67 D as the expected value for 1-tolylpyrrole (XI). The fairly

FIG. 1.

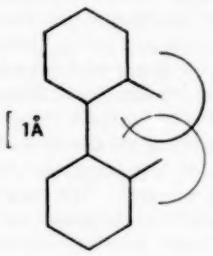


FIG. 2.

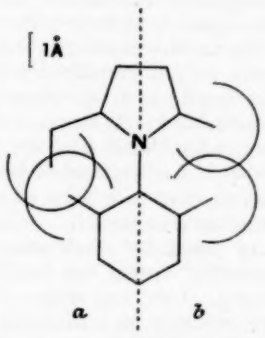
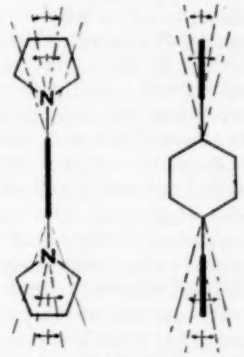


FIG. 3. *The pyrrole and benzene rings are shown orthogonally. The broken lines indicate the two modes of oscillation suggested for each pyrryl group and the bond attaching it to benzene.*



good agreement with the observed value 1·79 D shows that the resultant moment of 1-phenylpyrrole is positive and further suggests that the assumed collinearity of both compounds is correct. Non-collinearity would make the predicted value even smaller.

The moment calculated for 1-*p*-chlorophenylpyrrole (XIII) by a similar procedure, chlorobenzene being taken as 1·60 D, is −0·28 D. If allowance be made for the moments induced in chlorine by the pyrryl dipole and in the pyrrole ring by the C–Cl dipole this value becomes −0·31 D. The experimental figure is 0·3 D. Non-collinearity is therefore unlikely in the conjugated compounds.

Collinearity in the non-conjugated series may be tested by comparison of (VIII) with (XII). The value predicted for (XII) from that of (VIII) and the assumed extra moment 0·35 D of Me–$C_{ar.}$ is 2·35 D, collinearity being assumed. The observed value is 2·34 D. The component moment of Me–C is, however, too small for this test to be reliable. For this reason (XIV) and (XV), with the more polar halogen substituents, were investigated. From the observed moments of (VIII) and with chlorobenzene taken as 1·60 D, we get +0·40 D as the expected value for (XIV) if this be collinear. When allowance is made for induced moments, this value is reduced to +0·36. The observed value is 0·50 D, *i.e.*, it is larger than the predicted one. The same is true for the bromo-derivative (XV), where the respective values, the moment of bromobenzene being taken as 1·57 D, are +0·43 (uncorrected), +0·41 (corrected), and 0·54 D (observed). The discrepancy in the last two cases could arise from a small departure, about 6—7°, from collinearity.

The nitro-compound (XVI) has a moment of 2·48 D. The uncorrected calculated value, the moment of nitrobenzene being taken as 4·00 D, is −2·00 D, and the corrected one is 2·09 D. The discrepancy provides no evidence for non-collinearity, because electronic shifts involving the π-electrons of the nitro-group and of the pyrrole ring may well occur.

Because these results gave no clear answer, it was hoped that a direct test might be

made by measuring (XVII), which evidently would be non-polar if it were collinear. The observed moment is, however, 0·77 D. This may be real, *i.e.*, due to permanent non-collinearity of the molecule, or it may be an apparent moment due to atom polarization, which has been shown to reach considerable magnitudes in other *p*-disubstituted benzenes, or it may be due to each factor in part. It is possible that the 2 : 5-dimethylpyrryl groups oscillate as a whole owing to bending of the Ph–N valencies relatively to the axis of the benzene ring (Fig. 3), and further that the pyrrole rings themselves either (*a*) oscillate relatively to the N–Ph bonds or (*b*) are permanently bent relatively to them. Alternative (*a*) would give rise to two atom polarizations, and alternative (*b*) to an atom polarization and an orientation polarization, although the distinction in such cases is not an absolute one (cf. Sutton, *Ann. Reports*, 1940, **37**, 57 *et seq.*).

The first contribution may be estimated by assuming that each pyrryl group is a two-dimensional oscillator, that the oscillating moment μ_i is 2·0 D [that of compound (VIII)], and that the force constant is $V_i = 3 \times 10^{-12}$ erg/radian^2/molecule. From the relation $_AP = 4\pi N\mu_i^2/9V_i$ for each dimension of oscillation of each oscillator, we get an atom polarization $_AP = 4{\cdot}5$ c.c. The apparent orientation polarization, corresponding to the moment 0·77 D, which we have to explain is 12·1 c.c. The remaining 7·6 c.c. must then be due either to the second atom polarization or to the permanent bending about the ring nitrogen atom. In the former case we can calculate the force constant, by applying the same relation, regarding each pyrrole ring as a two-dimensional oscillator and taking the moment μ_i as 0·8 D [*i.e.*, that of compound (III) less an estimated 1·3 for the H–N bond]. This gives $V_i = 0{\cdot}28 \times 10^{-12}$ erg/radian^2/molecule, which is a very small value. In the latter case we can derive the angle θ of permanent bend relatively to the axis of the pyrrole ring, from the relation $2\mu_i \sin\theta = \sqrt{2}\,\mu_T$ where μ_T is the moment (0·6 D) corresponding to 7·6 c.c. of orientation polarization. This gives $\theta = 32°$. We conclude, therefore, either that there is an unusually small force constant of bending for the N–Ph bond relatively to the pyrrole ring, or that this bond is up to 32° permanently out of line with the axis of the pyrrole ring. Lord and Miller (*J. Chem. Physics*, 1942, **10**, 339) consider that there is spectroscopic evidence for a flattened potential curve for energy as a function of the inclination of the N–H bond in pyrrole to the ring plane. This would agree with the former of our alternative conclusions, which therefore we favour. For further elucidation the moment of *p*-phenylenedi-1-pyrrylbenzene (XVII without the methyl groups) should be useful. If this conjugated compound were to have moment of the same order of magnitude as that of (XVII) it would support the explanation on grounds of atom polarization only. If, on the other hand, the moment be decidedly smaller or zero, then the apparent moment of (XVII) is likely to be due to permanent bend. An attempt is being made to prepare the new compound.

The general conclusions from the tests carried out are that in 1-phenylpyrrole the ring axes are very probably collinear, but that in the compounds with sterically hindered conjugation (VIII, etc.) they probably are not more than 7° out of line, as judged from the values of the *p*-substituted derivatives. Even if the N–Ph bond in these is out of plane to this extent, this still means that there is clear evidence of a large degree of separation of the orbitals of the nitrogen atom into an sp^2 set used for σ-bonds and a *p*-orbital which participates in π-bonding within the pyrrole ring. The problem is the same as that which arises in the sydnones (cf. Hill and Sutton, *loc. cit.*).

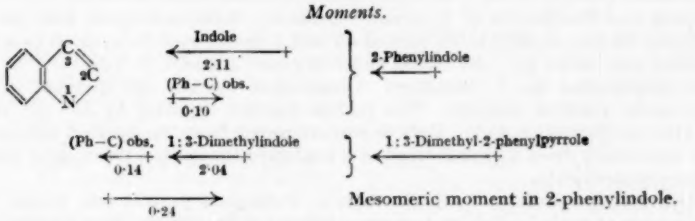
(*C*) *Steric Inhibition of Interannular Conjugation in the* 1-*Phenylpyrrole Series.*—In the series (VII)—(X) because of the increasing number of methyl groups in the positions *ortho* to the interannular link, the steric interference (cf. Fig. 3) should cause the benzene ring to be twisted about the N–Ph link out of the plane of the hetero-ring and thus inhibit the interannular conjugation more and more in the order given. The moments of (VIII), (IX), and (X) are directly comparable because the moments of the methyl groups in the benzene ring cancel; but in (VII) we must allow for the absence of the methyl groups in the 2 : 5-positions of the pyrrole ring. If we do this, on the basis of the substitution moments used previously, we obtain 1·54 D as the comparable value [*i.e.*, the moment predicted for (VIII) if it had been coplanar].

In (VII), with least if any steric influences, the positive moment of 1-phenylpyrrole

may be opposed by a negative π-moment, due to the interannular conjugation. The π-moment should progressively diminish in (VIII) and (IX). It probably vanishes in (IX) as shown by the near equality of the observed moments of (IX) and (X). The magnitude of the π-moment may be calculated, as the difference of the corrected moment of (VII), *i.e.*, 1·54 D, and the moment of (IX) or (X), to be −0·53 D. In this calculation we have assumed collinearity of all the compounds involved. A check on this value is obtained from the pair (VII) and (II), which should differ only by the π-moment, which therefore is −0·60 D.

The observed moments of (IV) and (IX) are identical, which is to be expected if the conjugation is completely inhibited in (IX) and if the effective σ-moments of Me–N and Ph–N are similar.

It would be interesting to compare the derived π-moment of *ca.* −0·5 D with that created by interannular conjugation when the benzene ring is attached to a *carbon* atom in pyrrole and not to the nitrogen. The present investigation does not include *C*-phenylpyrroles but results for indoles reported by Janetsky and Lebret (*loc. cit.*) permit of a rough calculation. The direction of the indole moment being taken to be approximately parallel to the radial bond from $C_{(2)}$ and in the sense shown in Fig. 1 (see p. 1471) the contribution of the Ph–C link is the difference between 2·11 D and 2·01 D, *i.e.*, $\mu_{C-Ph} = 0·10$. The Ph–C moment can also be calculated from 1 : 3-dimethylindole (2·04 D) and 1 : 3-dimethyl-2-phenylindole (2·18 D), to be $\mu_{Ph-C} = 0·14$ D, which is in the opposite direction. The reason for the difference in magnitude and direction of the two derived values is probably that 1 : 3-dimethyl-2-phenylpyrrole is similar to 2 : 5-dimethyl-1-phenylpyrrole in that steric influences twist the benzene ring out of the normal plane and inhibit the conjugation. The latter value, $\mu_{Ph-C} = 0·14$ D, may give the order of magnitude and direction of the extra σ-moment (relative to H–C) of the group Ph–C in indole and pyrrole. We conclude, therefore, that in the coplanar, conjugated compounds a π-moment of about 0·24 D in the opposite direction, C–Ph, is superimposed on it. These relations are shown in the vector diagram below.



(The direction of the mesomeric moment is that which would be expected from the increase of negative charge in the pyrrole ring.)

Conclusions.—The main conclusions we derive from the results are the following :

(i) The moments of pyrrole and of 1-methylpyrrole are certainly *positive*, *i.e.*, they have the positive pole toward the nitrogen atom and the negative one toward the rest of the ring atoms. This agrees with current explanations of the aromatic character of the pyrrole ring.

(ii) The observed moment of pyrrole agrees fairly well in magnitude with that calculated by a molecular-orbital procedure : the π-moment derived thereform is +1·40 D. The moment of 1-methylpyrrole indicates that the Me–N group moment is larger than in a tertiary aliphatic amine.

(iii) The N–H and N–Me bonds in pyrrole and 1-methylpyrrole are probably not much inclined to the plane of the ring. This also agrees with current theory.

(iv) The ring axes in 1-phenylpyrrole are very probably collinear, but in 2 : 5-dimethyl-1-phenylpyrrole they may be up to 7° out of line.

(v) *p*-Bis-(2 : 5-dimethyl-1-pyrryl)benzene (XVII) has a small apparent moment of 0·77 D. If this is due to atom polarization the force constant for the bending of the pyrryl

group relatively to the benzene ring must be abnormally small. If it is a real moment, the pyrrole and the phenyl axes are about 32° out of line. The former alternative agrees with the spectroscopic evidence for the structure of pyrrole itself.

(vi) In 1-phenylpyrrole there is a π-moment of about −0·5 D, due to interannular conjugation. It is reduced by substituting methyl groups for hydrogen in the 2 : 5-positions of the pyrrole ring and in the *o*-positions of the benzene ring. Methyl groups in the 2 : 5-positions stop it almost completely, and one more methyl group in an *o*-position does so quite completely.

(vii) There are small induced moments in 2 : 5-dimethyl-1-*p*-nitrophenylpyrrole and probably a considerable electromeric interaction moment.

Experimental

Physical Measurements.—All measurements were made at 25°. The electric dipole moment was obtained from the equation $\mu = 0{\cdot}2212({}_{T}P - R_D)^{\frac{1}{2}}$. No correction was made for atom polarization apart from that implied in using R_D to give the distortion polarization. The total polarization ${}_{T}P$ was computed from the observed values of dielectric constant, and the specific volume for benzene solutions by Halverstadt and Kumler's procedure (*J. Amer. Chem. Soc.*, 1942, **64**, 2988). Symbols have the same significance as in that paper. The dielectric constants ε were measured with a heterodyne beat capacity meter designed by R. A. W. Hill and L. E. Sutton in conjunction with a condenser similar to that described by Jenkins and Sutton (*J.*, 1935, 609). Specific volumes were measured with a modified Sprengel–Ostwald pyknometer. The molar refractions R_D were computed from the refractive indices and specific volumes usually only from the most concentrated solutions, as most of the compounds have refractive indices close to that of benzene itself.

The refractive index n_D of the solution relative to that of the benzene used for preparing it was measured with a Pulfrich refractometer fitted with a centrally divided cell. The standard dielectric constant of pure dry benzene was taken as 2·2727 (Hartshorn and Oliver, *Proc. Roy. Soc.*, 1929, **123**, *A*, 664).

The results are given in Table 2, all dipole moments being in Debye units.

Preparation and Purification of Materials.—Benzene. Analytical-grade benzene was frozen out three times, about one-fifth being poured off and rejected each time, dried over phosphoric oxide, distilled just before use, and stored under dry air; it had f. p. 5·2°.

Pyrrole (preparation by J. Jackson). Commerical pyrrole was distilled in a coal-gas atmosphere under reduced pressure. The middle fraction distilling at 31—32°/17 mm. was converted into the potassium salt. Pyrrole was recovered from the purified salt by treatment with water and finally dried and redistilled in a coal-gas atmosphere, the middle fraction being used for the measurements.

1-*Methylpyrrole* (preparation by J. Jackson). Potassium pyrrole was boiled for 6 hours with 2 equivalents of methyl iodide and an equal volume of dry ether. The product was isolated by fractional distillation and, after a final treatment with metallic sodium, was redistilled in a coal-gas atmosphere under reduced pressure; it had b. p. 20°/17 mm. (yield 40%) (Found: N, 17·4. Calc. for C_5H_7N: N, 17·3%).

2 : 5-*Dimethylpyrrole.* This was prepared by refluxing acetonylacetone with ammonium carbonate (*Org. Synth.*, Coll. Vol. II, p. 219). After isolation the product was distilled under reduced nitrogen pressure. The constant-boiling middle fraction distilled at 74°/19 mm. It was twice frozen out in a nitrogen atmosphere, one-fourth being poured off and rejected each time. The product was stored in a glass container which was sealed off, after being filled with nitrogen. It had n_D^{25} 1·4980 (n_D^{22} 1·500, *loc. cit.*), and remained colourless until exposed to air. The measurements were carried out in a nitrogen atmosphere.

1 : 2 : 5-*Trimethylpyrrole.* An attempt was made to prepare this compound by refluxing acetonylacetone with methylammonium chloride at 100°. The mixture turned green, and no condensation took place in neutral conditions. A successful preparation was carried out as follows. Acetonylacetone and methylammonium chloride (0·2 mole each) in water (20 ml.), were treated with aqueous sodium hydroxide (0·4 mole in 20 ml.) dropwise, at <0°. The reaction mixture was finally heated for a few minutes, and the oily layer isolated, washed with water, dried and distilled. The substance, b. p. 68°/17 mm., was stored in a sealed tube. It is more stable to air and light than the previous compound. Knorr (*Annalen*, 1886, **236**, 304) gives b. p. 170°/760 mm., 169°/746 mm.

TABLE 2. (Roman numerals refer to Table 1).

Pyrrole (I)

$10^5\omega$	ε	v	${}_TP$	$10^5\Delta n^D_{25}$
157	2·2800	—	—	—
320	2·2898	—	87·4	—
716	2·3111	1·14360	87·0	—
1028	2·3268	1·14328	85·9	—
1487	2·3514	—	85·4	—
2033	2·3812	1·14185	85·5	—

$\varepsilon = 2{\cdot}2720 + 5{\cdot}376\omega$; $v = 1{\cdot}14456 - 0{\cdot}1323\omega$;
${}_TP = 88{\cdot}0$ c.c.; $R_D = 21{\cdot}7$ c.c.; $\mu = 1{\cdot}80 \pm 0{\cdot}01$ D

1-*Methylpyrrole* (II)

258	2·2896	1·14390	104·5	—
492	2·2977	1·14380	103·6	—
742	2·3103	1·14371	103·1	—
1480	2·3468	1·14336	101·5	—
2309	2·3895	1·14300	101·6	—

$\varepsilon = 2{\cdot}2747 + 4{\cdot}929\omega$; $v = 1{\cdot}14401 - 0{\cdot}0428\omega$;
${}_TP = 101{\cdot}7$ c.c.; $R_D = 26{\cdot}7$ c.c.; $\mu = 1{\cdot}92 \pm 0{\cdot}02$ D

2 : 5-*Dimethylpyrrole* (III)

283	2·2849	1·14539	—	—
560	2·3003	1·14513	—	—
856	2·3134	1·14500	—	—
1468	2·3438	1·14446	—	00

$\varepsilon = 2{\cdot}2717 + 4{\cdot}918\omega$; $v = 1{\cdot}14563 - 0{\cdot}0802\omega$;
${}_TP = 118{\cdot}2$ c.c.; $R_D = 29{\cdot}8$ c.c.; $\mu = 2{\cdot}08 \pm 0{\cdot}03$ D

1 : 2 : 5-*Trimethylpyrrole* (IV)

189	2·2809	1·14511	—	—
446	2·2921	1·14502	—	—
568	2·2970	1·14496	—	—
1196	2·3238	1·14478	—	00

$\varepsilon = 2{\cdot}2730 + 4{\cdot}254\omega$; $v = 1{\cdot}14517 - 0{\cdot}0328\omega$;
${}_TP = 123{\cdot}5$ c.c.; $R_D = 35{\cdot}8$ c.c.; $\mu = 2{\cdot}07 \pm 0{\cdot}01$ D

3 : 4-*Di-iodo*-2 : 5-*dimethylpyrrole* (V)

116	2·2789	1·14433	—	—
375	2·2922	1·14243	—	—
540	2·3008	1·14129	—	32
1143	2·3322	1·13679	—	76

$\varepsilon = 2{\cdot}2727 + 5{\cdot}199\omega$; $v = 1{\cdot}14518 - 0{\cdot}7311\omega$;
${}_TP = 382{\cdot}2$ c.c.; $R_D = 55{\cdot}5$ c.c.; $\mu = 4{\cdot}00 \pm 0{\cdot}01$ D

2 : 3 : 4 : 5-*Tetraiodopyrrole* (VI)

109	2·2748	1·14421	—	—
238	2·2759	1·14288	—	—
586	2·2815	1·13986	—	50
1091	2·2887	1·13566	—	86

$\varepsilon = 2{\cdot}2729 + 1{\cdot}443\omega$; $v = 1{\cdot}14502 - 0{\cdot}864\omega$;
${}_TP = 202{\cdot}7$ c.c.; $R_D = 72{\cdot}7$ c.c.; $\mu = 2{\cdot}52 \pm 0{\cdot}04$ D

1-*Phenylpyrrole* (VII)

80	2·2745	1·14489	—	—
191	2·2771	1·14471	—	20
435	2·2808	1·14442	—	—
773	2·2859	1·14363	—	76

$\varepsilon = 2{\cdot}2736 + 1{\cdot}610\omega$; $v = 1{\cdot}4508 - 0{\cdot}180\omega$;
${}_TP = 84{\cdot}1$ c.c.; $R_D = 48{\cdot}7$ c.c.; $\mu = 1{\cdot}32 \pm 0{\cdot}04$ D

2 : 5-*Dimethyl*-1-*phenylpyrrole* (VIII)

104	2·2759	1·14532	—	—
288	2·2812	1·14501	—	—
699	2·2920	1·14444	—	41

$\varepsilon = 2{\cdot}2732 + 2{\cdot}691\omega$; $v = 1{\cdot}14545 - 0{\cdot}145\omega$;
${}_TP = 137{\cdot}6$ c.c.; $R_D = 56{\cdot}1$ c.c.; $\mu = 2{\cdot}00 \pm 0{\cdot}04$ D

2 : 5 : 2′ : 5′-*Tetramethyl*-1-*phenylpyrrole* (IX)

$10^5\omega$	ε	v	${}_TP$	$10^5\Delta n^D_{25}$
212	2·2780	1·14485	—	—
351	2·2812	1·14460	—	—
829	2·2930	1·14438	—	—
1443	2·3078	1·14374	—	57

$\varepsilon = 2{\cdot}2728 + 2{\cdot}429\omega$; $v = 1{\cdot}41505 - 0{\cdot}0937\omega$;
${}_TP = 153{\cdot}4$ c.c.; $R_{D_\infty} = 66{\cdot}2$ c.c.; $\mu = 2{\cdot}07 \pm 0{\cdot}02$ D

2 : 5 : 2′ : 4′ : 6′-*Pentamethyl*-1-*phenylpyrrole* (X)

273	2·2786	1·14496	—	—
684	2·2875	1·14460	—	—
837	2·2917	1·14450	—	—
1316	2·3019	1·14402	—	44

$\varepsilon = 2{\cdot}2725 + 2{\cdot}241\omega$; $v = 1{\cdot}14523 - 0{\cdot}0916\omega$;
${}_TP = 156{\cdot}8$ c.c.; $R_D = 70{\cdot}2$ c.c.; $\mu = 2{\cdot}06 \pm 0{\cdot}04$ D

1-p-*Tolylpyrrole* (XI)

80	2·2752	1·14489	—	—
370	2·2815	1·14446	—	—
418	2·2828	1·14444	—	—
874	2·2940	1·14345	—	55

$\varepsilon = 2{\cdot}2730 + 2{\cdot}388\omega$; $v = 1{\cdot}14510 - 0{\cdot}182\omega$;
${}_TP = 115{\cdot}6$ c.c.; $R_D = 50{\cdot}1$ c.c.; $\mu = 1{\cdot}79 \pm 0{\cdot}04$ D

2 : 5 : 4′-*Trimethyl*-1-*phenylpyrrole* (XII)

69	2·2746	1·14526	—	—
311	2·2827	1·14500	—	—
662	2·2943	1·14459	—	30

$\varepsilon = 2{\cdot}2723 + 3{\cdot}328\omega$; $v = 1{\cdot}14532 - 0{\cdot}107\omega$;
${}_TP = 173{\cdot}3$ c.c.; $R_D = 61{\cdot}2$ c.c.; $\kappa = 2{\cdot}34 \pm 0{\cdot}02$ D

1-p-*Chlorophenylpyrrole* (XIII)

114	2·2731	1·14503	—	—
180	2·2736	1·14485	—	—
422	2·2742	1·14427	—	—
722	2·2745	1·14333	—	36

$\varepsilon = 2{\cdot}2732 + 0{\cdot}207\omega$; $v = 1{\cdot}14540 - 0{\cdot}2857\omega$;
${}_TP = 52{\cdot}4$ c.c.; $R_D = 50{\cdot}2$ c.c.; $\mu = 0$—$0{\cdot}3$ D

1-p-*Chlorophenyl*-2 : 5-*dimethylpyrrole* (XIV)

105	2·2728	1·14492	—	—
275	2·2734	1·14450	—	—
674	2·2749	1·14332	—	44
1046	2·2756	1·14203	—	66

$\varepsilon = 2{\cdot}2726 + 0{\cdot}310\omega$; $v = 1{\cdot}14530 - 0{\cdot}306\omega$;
${}_TP = 63{\cdot}4$ c.c.; $R_D = 58{\cdot}2$ c.c.; $\mu = 0{\cdot}50 \pm 0{\cdot}04$ D

1-p-*Bromophenyl*-2 : 5-*dimethylpyrrole* (XV)

163	2·2733	1·14450	—	—
229	2·2733	1·14420	—	—
557	2·2743	1·14278	—	38
1057	2·2759	1·14074	—	67

$\varepsilon = 2{\cdot}2727 + 0{\cdot}309\omega$; $v = 1{\cdot}14514 - 0{\cdot}414\omega$;
${}_TP = 69{\cdot}0$ c.c.; $R_D = 62{\cdot}9$ c.c.; $\mu = 0{\cdot}54 \pm 0{\cdot}03$ D

2 : 5-*Dimethyl*-1-p-*nitrophenylpyrrole* (XVI)

136	2·2774	1·14459	—	—
331	2·2834	1·14410	—	—
472	2·2883	1·14344	—	38
884	2·3022	1·14242	—	73

$\varepsilon = 2{\cdot}2727 + 3{\cdot}321\omega$; $v = 1{\cdot}14500 - 0{\cdot}299\omega$;
${}_TP = 189{\cdot}5$ c.c.; $R_D = 64{\cdot}1$ c.c.; $\mu = 2{\cdot}48 \pm 0{\cdot}02$ D

p-*Bis*-(2 : 5-*dimethyl*-1-*pyrryl*)*benzene* (XVII)

173	2·2731	1·14475	—	—
377	2·2747	1·14451	—	—
648	2·2751	1·14379	—	47
964	2·2771	1·14315	—	73

$\varepsilon = 2{\cdot}2725 + 0{\cdot}456\omega$; $v = 1{\cdot}14523 - 0{\cdot}218\omega$;
${}_TP = 95{\cdot}6$ c.c.; $R_D = 83{\cdot}5$ c.c.; $\mu = 0{\cdot}77 \pm 0{\cdot}03$ D

2 : 3 : 4 : 5-*Tetraiodopyrrole.* This was prepared according to Ciamician and Silber (*Ber.*, 1885, **18**, 1766) by iodination of pyrrole in alkaline aqueous solution. It is essential in order to avoid formation of tar that the iodine solution be added dropwise no faster than it is consumed : even then the product is strongly coloured. It was recrystallized (charcoal) several times. The final product was slightly yellow; it decomposed without melting at 150—160° [Found : N, 2·6; I, (82·2), 88·7. Calc. for C_4HNI_4 : N, 2·5; I, 89·0%].

3 : 4-*Di-iodo*-2 : 5-*dimethylpyrrole.* On attempted direct iodination in neutral aqueous solution, partial decomposition and precipitation of a heavy brown oil occurred. In an alkaline medium (1·9 g. of 2 : 5-dimethylpyrrole, 2 g. of sodium hydroxide in 50 ml. of 50% ethanol) the substance readily takes up the calculated amount of iodine, and white heavy crystals appear. (Undoubtedly the hydrogen iodide set free during iodination in initially neutral solution causes the coloration.) Recrystallized several times from 50% alcohol, the *compound* had m. p. 123—124° (decomp.) (Found : N, 4·0; I, 73·5. $C_6H_7NI_2$ requires N, 4·0; I, 73·2%).

2 : 5-*Dimethyl*-1-*phenylpyrrole.* Ethyl diacetylsuccinate was prepared as described by Fischer (" Anleitung zur Darstellung Organischer Präparate," 1920, 48). It was condensed with aniline in glacial acetic acid (Knorr, *Annalen*, 1886, **236**, 305). The ethyl 2 : 5-dimethyl-1-phenylpyrrole-3 : 4-dicarboxylate was hydrolysed and decarboxylated. The product, recrystallized twice from alcohol, had m. p. 49—50° (Knorr, *loc. cit.*, gives 51°).

1-*Phenylpyrrole.* This was prepared by Köttnitz's method (*J. pr. Chem.*, 1873, **6**, 143), *i.e.*, by pyrolysis of anilinium mucate. On being twice recrystallized from alcohol, it was obtained as white leaflets, m. p. 60—61° (Köttnitz, *loc. cit.*, gives 62°).

1-p-*Tolylpyrrole.* This was prepared similarly and recrystallized from alcohol as white crystals, m. p. 82—82·5° (Pictet, *Ber.*, 1904, **37**, 2795, gives 82°).

1-p-*Chlorophenylpyrrole.* By the same method, this compound was prepared; recrystallized twice from alcohol, it had m. p. 87—88° (Wibaut and Dhont, *Rec. Trav. chim.*, 1933, **62**, 272, report 88—89°).

2 : 5 : 2′ : 5′-*Tetramethyl*-1-*phenylpyrrole.* This and the following compounds were prepared according to Hazlewood, Hughes, and Lions's method (*J. Proc. Roy. Soc. New South Wales*, 1937, **71**, 92), *i.e.*, condensation of the appropriate amine with acetonylacetone, catalysed by a few drops of 5N-hydrochloric acid. Commerical *p*-xylidine, free from *m*-4-xylidene, was distilled at 214°/760 mm., and condensed with acetonylacetone. The product distilled at 148—149°/45 mm. (Hazlewood *et al.*, *loc. cit.*, give 121°/9 mm.).

2 : 5 : 2′ : 4′ : 6′-*Pentamethyl*-1-*phenylpyrrole.* Nitromesitylene, prepared essentially according to *Org. Synth.*, Coll. Vol. II, p. 449, by nitration of commercial mesitylene, was reduced with tin and hydrochloric acid. A complex was precipitated as dark red crystals. It was decomposed by alkali, and the amine isolated by steam-distillation as a slightly yellow product and dried. The b. p. was 233°/760 mm. This product was then condensed with acetonylacetone, the reaction proceeding smoothly at 100°. The product was obtained in good yield as a colourless liquid which distilled constantly at 134—135°/11 mm. (Found : C, 84·4; H, 9·0. $C_{15}H_{19}N$ requires C, 84·5; H, 8·9%).

2 : 5-*Dimethyl*-p-*tolylpyrrole.* Prepared from *p*-toluidine, this formed white crystals, m. p. 45—46° (Knorr, *loc. cit.*, gives 45—46°).

1-*p*-Chlorophenyl-2 : 5-dimethylpyrrole, similarly prepared from *p*-chloroaniline, formed white crystals, m. p. 49—50° (Hazlewood *et al.*, *loc. cit.*, give 50°); the *p*-bromo-compound, from *p*-bromoaniline, formed white crystals, m. p. 74·5—75° (74—75°, *loc. cit.*); and the *p*-nitro-compound, from *p*-nitroaniline, formed yellow crystals, m. p. 145° (145°, *loc. cit.*).

p-Bis-(2 : 5-dimethyl-1-pyrryl)benzene, from *p*-phenylenediamine, recrystallized from benzene as white crystals, m. p. 255—257° (Hazlewood *et al.*, *loc. cit.*, give 245—253°) (Found : C, 81·9; H, 7·4. Calc. for $C_{18}H_{20}N_2$: C, 81·8; H, 7·6%).

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270. *The Photochemical Decomposition of Keten by Means of Light of Very High Intensity.*

By K. KNOX, R. G. W. NORRISH, and G. PORTER.

The photochemical decomposition of keten has been studied by using a flash-discharge lamp with a useful output of 10^{23} quanta/second and an effective duration of 1·5 milliseconds.

At low intensities, or in the presence of a large excess of inert gas, the products are mainly carbon monoxide and ethylene as found under normal photolysis conditions. As the intensity is increased, or the inert-gas pressure decreased, hydrogen and acetylene are formed in increasing amounts until eventually they, with some carbon, become the major products and the quantum yield of keten decomposition increases to a value of over 6. This change is shown to be caused by the adiabatic nature of the photolysis, the short times involved and high radical concentration resulting in a very high temperature followed by rapid quenching of the reaction. By analysis of the products under different conditions of intensity, pressure, and dilution, it is possible to follow the course of the complex reactions taking place, and the results show fairly clearly that carbon formation takes place by successive dehydrogenation of C_2 hydrocarbons, followed by polymerisation to graphite. Higher hydrocarbons and polymers are almost absent from the products of the high-intensity decomposition and in excess of methane the first hydrocarbon formed is ethane.

Attempts to obtain the absorption spectrum of methylene are discussed in relation to this work.

IN a preliminary note we have described the effects of very high intensity radiation on several well-known photochemical reactions (Norrish and Porter, *Nature*, 1949, **164**, 658). It is essential that these effects should be understood if full advantage is to be taken of the high radical and atom concentrations which are obtained by use of the flash discharge and which make possible the study of free-radical reactions by direct methods such as absorption spectroscopy (Porter, *Proc. Roy. Soc.*, 1950, *A*, **200**, 284; *Discuss. Faraday Soc.*, 1950, **9**, 60). A detailed analysis of the products of photolysis of keten, by aid of the flash discharge, has therefore been undertaken with the primary object of testing the hypotheses originally put forward to explain the effects of high-intensity radiation. Keten was chosen because of our interest in two special aspects of this sytem: first, the methylene radical which has so far eluded all attempts at detection by absorption spectroscopy and, secondly, the mechanism of carbon formation in the homogeneous gas phase. The latter is of great importance but is not suitable for study in photochemical reactions at normal intensities.

EXPERIMENTAL

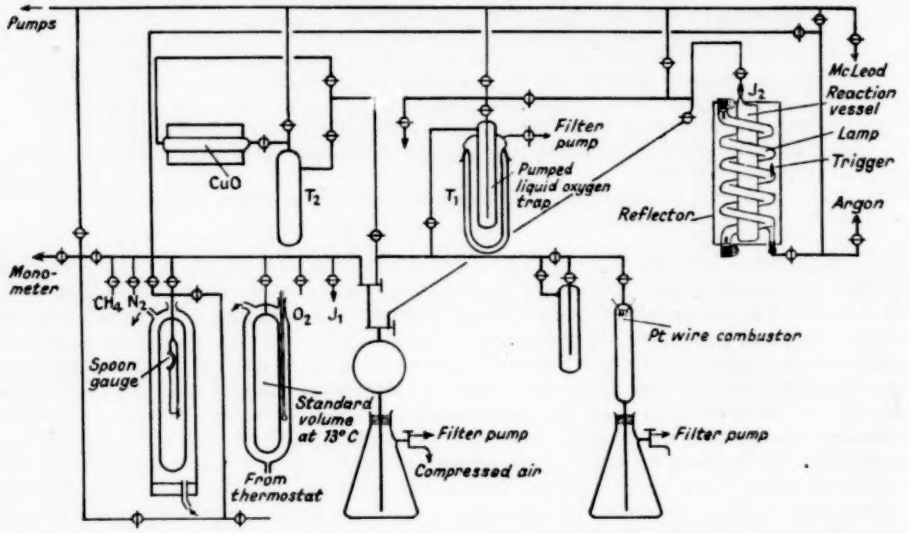
Keten, prepared by pyrolysis of acetone (Hurd and Tallyn, *J. Amer. Chem. Soc.*, 1925, **47**, 1427), was purified by three distillations between traps at −111°, −139°, and −196°, a small fraction being collected in the middle trap. It was stored under liquid nitrogen, where it could be kept indefinitely without changing composition. Analysis, by combusion in excess of oxygen and by absorption on potassium hydroxide, indicated a purity of 98%. Nitrogen was prepared by decomposition of sodium azide, using Justi's procedure (*Ann. Physik*, 1931, **10**, 983), which gives an extremely pure product. Methane, from a cylinder, was condensed in a trap surrounded by liquid oxygen pumped down to a pressure of 10 cm. Hg where its temperature was about −198°. Most of the condensate was pumped away, and half the residue was expanded into a bulb by allowing the trap to warm. Combustion showed a purity of greater than 99% of methane. Oxygen was prepared electrolytically, dried ($CaCl_2$), passed over platinised asbestos heated to 350°, and finally again dried (P_2O_5).

The apparatus used in these experiments, consisting of the flash lamp and reaction vessel with associated gas-handling and gas-analysis equipment, is shown in Fig. 1. The flash lamp is similar in construction to that described by Porter (*loc. cit.*) except that here the metre tube

is coiled around a quartz reaction vessel of 125-c.c. capacity, the whole being surrounded by a reflector coated with magnesium oxide. The tube was evacuated to 10^{-6} mm. Hg and refilled with argon to a pressure of 10 cm. Hg before each flash, and the energy from a 480 μF bank of condensers, charged to 4000 v, was used in all these experiments. A single flash has a duration of 1·5 milliseconds, during which more than 10^{20} quanta are dissipated between 2000 and 5000 Å, as determined by uranyl oxalate actinometry.

The pressures of reactant and product gases were always measured in the thermostated standard volume at a temperature of 13° by means of a spoon gauge. After the flash, the gaseous products were pumped into trap T_1, surrounded by liquid oxygen at a temperature of about −198°. The non-condensable gases, consisting of hydrogen, carbon monoxide, methane, and nitrogen if present, were transferred to the standard volume for pressure measurement, and then to the tube containing copper oxide at 300°. There, hydrogen and carbon monoxide were oxidised, and the resulting water and carbon dioxide condensed out in trap T_2 by liquid air, the methane and any nitrogen being returned to the standard volume for pressure measurement. Combustion in excess of oxygen showed this residue to be in fact methane

FIG. 1. *General arrangement of photolysis and analysis apparatus.*



(besides any nitrogen). The liquid air around trap T_2 was replaced by a dry ice–acetone mixture, and the carbon dioxide drawn off and measured. Hydrogen was calculated by difference. Trap T_1 was then allowed to warm to room temperature, and the condensables were transferred from it into the standard volume and their pressure read. Excess of keten was removed by absorption on a succession of potassium hydroxide beads and the gases were then condensed into an evacuated bulb attached to the apparatus at joint J_1 and removed to the capillary burette shown in Fig. 2.

The residual gases were now analysed for acetylene by absorption on cuprous chloride and for ethylene and propylene together by fuming sulphuric acid, by the usual microtechnique (Farkas and Melville, " Experimental Methods in Gas Reactions," Macmillan, 1939, p. 183). The small amount of remaining gas was assumed to be ethane, since combustion analysis of the condensable mixture had shown that C_2 compounds were present almost exclusively. In the runs made in the presence of methane this residue was relatively large and a combustion analysis was made to verify that it was ethane.

In order to analyse any carbon deposited and polymer formed, a measured amount of excess of oxygen was admitted to the reaction vessel and the full heat of a Bunsen burner was played on the walls of the vessel. This was found to oxidise the deposit completely to carbon dioxide and water. By the usual separations with liquid nitrogen and with dry ice–acetone, the oxygen used and carbon dioxide produced were determined.

The analyses of the carbon deposits from individual runs, showing that slightly more oxygen was consumed than appeared in the carbon dioxide produced, led to the belief that the deposit might consist of some hydrogen-containing polymer in addition to the elementary carbon. This was confirmed by tests for water, which were positive though not, of course, suitable for quantitative estimation. The figures given for hydrogen in the solid products are calculated from the oxygen deficiency.

Combustion analyses were carried out in the usual way, a 5-fold excess of oxygen being used. Sample and oxygen pressures were measured in the standard volume, and the gas transferred to the combustion vessel where complete combustion was obtained by heating the platinum wire to redness. The gases were then removed, first *via* a liquid-air trap, and then *via* a carbon dioxide–acetone trap, and the oxygen and carbon dioxide pressures measured in the standard volume. Tests with known mixtures showed these methods of analysis to be reliable.

In view of the appreciable amount of carbon dioxide found among the products of the

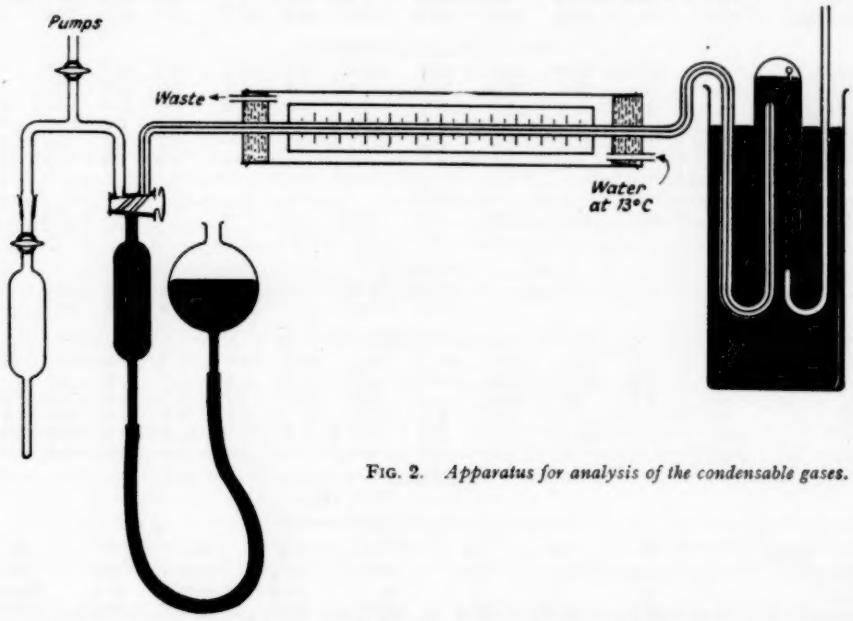


FIG. 2. *Apparatus for analysis of the condensable gases.*

thermal decomposition of keten by Akeroyd (Thesis, Cambridge Univ., 1936), a test was made for this gas in our experiments. The keten was removed by an amount of water which was too small to dissolve a significant volume of carbon dioxide, and this was then determined by absorption in potassium hydroxide.

RESULTS

Analysis of the gaseous products revealed the presence of methane and, at high decompositions, relatively large amounts of hydrogen. Combustion of the condensable gases showed that they consisted of C_2 hydrocarbons almost exclusively. The gaseous products were also investigated by infra-red and ultra-violet spectroscopy. Infra-red analysis indicated large amounts of acetylene in the hydrocarbon products from high-decomposition runs, as well as ethylene, but only a very small trace of propylene and no absorption by other molecules. Ultra-violet investigations showed that aromatic hydrocarbons were entirely absent, the products being investigated in a 1-m. absorption path under conditions such that less than 1% of benzene, toluene, etc., would have been easily detected. Analysis proved the absence of carbon dioxide, and combustion of the solid products showed that a small amount of hydrogen was present in addition to carbon.

Complete analyses of the products for CO, CH_4, H_2, C_2H_6, C_2H_4, C_2H_2, carbon, and hydrogen in the solid were now carried out under a variety of conditions. The reproducibility of the

analyses was satisfactory, but the percentage decomposition under identical conditions showed variations which were sometimes greater than analytical errors. In particular, there was a definite trend with time, the decomposition decreasing with the age of the lamp. It was thought that this might be caused by poisoning of the gas filling and, in an attempt to improve the reproducibility, the lamp was freshly filled with gas before each run. It is now known, in the light of detailed investigations on the properties of these lamps (Christie and Porter, in course of publication), that better reproducibility is obtained by using the same gas filling, the decrease in output of the lamp being caused by reduced transparency of the quartz, mainly by deposition of the material of the electrodes. Very good reproducibility of output is obtained

TABLE 1. *Low light intensity.*

Run	51	41	30	31	32	36	38	43	45	35	34	46
P (CH_2:CO) ...	10·0	29·5	59·1	60·3	59·8	90·2	90·3	90·5	180·3	60·0	60·0	60·0
P (N_2)	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	29·9	60·6	297·2
Decompn., %	39·6	64·4	61·8	58·4	58·6	24·0	24·6	27·2	6·0	41·1	27·6	7·5
Pressures of gaseous products :												
P (CO)	4·0	19·0	36·5	35·2	35·0	21·6	22·2	24·7	10·7	24·7	16·6	4·5
P (H_2)	0·9	7·9	19·1	13·3	16·3	3·6	2·3	2·8	0·0	3·8	0·9	—
P (CH_4)	0·0	1·3	2·4	3·8	2·8	2·1	3·0	3·0	0·0	2·1	0·0	0·0
P (C_2H_2)	0·45	7·2	10·4	5·6	6·2	1·5	6·4	2·1	0·1	2·4	1·1	0·2
P (C_2H_4)	0·70			2·4	2·0	4·1		4·9	3·7	4·0	4·1	1·5
P (C_2H_6)	0·17			0·5	0·7	0·9		0·6	0·3	1·3	1·3	0·4
Solid :												
P (C_3)	*	small	large	large	5·5	1·6	1·1	1·5	*	1·4	0·4	*
P (H_2)	—	—	—	—	0·8	0·4	0·0	0·0	—	0·8	0·2	—
Balances :												
C_2	3·3	—	—	—	33·3	20·0	19·0	23·0	9·5	22·5	15·2	4·4
H_2	3·3	—	—	—	34·3	20·6	—	22·5	7·4	21·8	14·3	4·4
Gaseous products, %												
CO	63·6	53·7	53·1	57·9	54·9	63·2	65·5	64·8	72·2	63·3	67·7	61·5
H_2	15·2	22·3	27·8	21·8	26·7	11·5	6·8	7·4	0·0	11·6	5·4	—
CH_4	0·0	3·7	4·1	6·3	4·3	6·0	8·9	7·9	0·0	5·3	0·0	0·0
C_2H_2	7·3	20·3	15·1	9·2	9·8	4·4	18·9	5·4	0·8	6·3	4·6	2·6
C_2H_4	11·2			4·0	3·2	12·1		12·9	24·8	10·1	16·9	20·5
C_2H_6	2·7			0·9	1·1	2·7		1·5	2·3	3·4	5·4	5·1

* Invisible.

TABLE 2. *High light intensity.*

Run	52	53	54	58	56	59	57	55
P (CH_2:CO)	60·2	60·6	10·0	10·0	10·4	10·0	10·2	10·5
P (N_2)	0	0	0	0	20·5	19·6	83·4	320·3
Decompn., %	90·7	91·0	94·3	90·6	92·7	92·5	88·9	82·1
Pressure of gaseous products :								
P (CO)	54·6	55·1	9·4	9·0	9·6	9·2	9·0	8·7
P (H_2)	35·5	37·3	5·3	5·1	4·5	5·1	2·4	0·2
P (CH_4)	0·6	0·2	0·2	0·0	0·0	0·0	0·4	0·4
P (C_2H_2)	13·9	13·7	3·6	3·4	4·7	4·0	1·9	1·1
P (C_2H_4)	0·2	0·4	0·04	0·08	0·2	0·2	0·9	1·8
P (C_2H_6)	0·6	0·4	0·15	0·15	0·4	0·3	0·4	0·6
Solid :								
P (C_3)	large	9·2	small	0·5	small	0·5	invisible	invisible
P (H_2)	—	1·4	—	0·0	—	0·0	—	—
Balances :								
C_2	—	51·4	8·6	8·6	10·1	9·1	7·9	8·1
H_2	—	54·8	9·8	9·1	10·8	10·4	8·1	7·5
Gaseous products, % :								
CO	51·8	51·0	50·5	51·0	49·5	49·4	60·0	67·6
H_2	33·7	35·8	28·3	28·7	23·3	27·2	16·3	1·5
CH_4	0·6	0·2	1·0	0·0	0·0	0·0	2·5	2·9
C_2H_2	13·2	12·3	19·2	19·1	24·3	21·2	12·5	8·8
C_2H_4	0·2	0·3	0·2	0·4	1·0	0·8	6·3	14·7
C_2H_6	0·6	0·3	0·8	0·8	1·9	1·3	2·5	4·4

if the energy per flash is slightly reduced, to about 3000 joules per flash, and the same gas filling is used throughout. The variation in decomposition between similar runs is not more than a few units %, however, which is not serious for the present purpose. The data in Table 1 are obtained with a lamp whose intensity had been considerably reduced. In Table 2 the same lamp was used after being cleansed with hydrofluoric acid, resulting in a higher intensity.

TABLE 3. *Effect of added methane at constant total pressure.*

Run	46	50	49
P (CH_2:CO)	60·0	60·8	60·2
P (CH_4)	0	120·3	300·4
P (N_2)	297·2	180·9	0
Decompn., %	7·5	7·4	10·6
Products :			
P (CO)	4·5	4·5	6·4
P (H_2)	0·8	0·0	0·0
P (CH_4)	0·0	115·2	292·7
P (C_2H_2)	0·2	0·13	0·1
P (C_2H_4)	1·5	1·43	2·1
P (C_2H_6)	0·4	1·45	4·4

The details of the analysis of the products of decomposition are given in Tables 1 and 2 for the low- and high-intensity lamps respectively, and in each case the effect of keten pressure and of the addition of nitrogen are studied. In Table 3 the effect of added methane is given, the total pressure $P(CH_4 + N_2)$ being constant. The balances C_2 and H_2 are the sum of carbon and hydrogen in the products, and are to be compared with the pressure of carbon monoxide produced representing the keten decomposed. Keten polymer, formed as solid, was negligible, as shown in the combustion analyses and also by the agreement found between keten removed and carbon monoxide produced. The balances show that no other major products were present.

All pressures in Tables 1, 2, and 3 are expressed in mm. of mercury in the reaction volume of 125 c.c. and at 13°.

In view of the interest in the mechanism by which carbon is formed in this reaction, the structure of the deposit was investigated with the aid of an electron microscope. The carbon particles were found to be fairly uniform in size, the average dimensions being about 500 Å, though most of them form agglomerations of large size. A few of the smaller particles showed definite diffraction patterns characteristic of graphitic structure and the whole deposit closely resembled those obtained from smoky acetylene flames.

Determination of Quantum Yield.—The effect of nitrogen in reducing the total decomposition under otherwise identical conditions suggests that, in the absence of nitrogen, the quantum yield must be in excess of the value found under ordinary conditions, which is of the order of unity.

The measurement of quantum yields in a flash decomposition such as this presents several new problems, but recent work by Christie and Porter (in course of publication) has shown that the methods of uranyl oxalate actinometry are applicable to the high intensities obtained with the flash discharge and that the quantum yield is unchanged. This makes possible the determination of the quantum yield of keten decomposition at high intensity, but the usual technique, of measuring the reduction in oxalate decomposition when a second cell containing the keten is interposed between the oxalate and the lamp, is unsuitable, owing to the fact that it involves the measurement of a small difference in two small decompositions. The method used, though more involved, is capable of greater accuracy. The quantity determined is the number of keten molecules decomposed divided by the total number of quanta absorbed in the region between 2000 and 4000 Å, it being impossible to obtain the high decomposition required by using a smaller wave-length range.

It was necessary to use a different optical arrangement, which gave an approximately parallel beam of light, for these experiments. The flash lamp was of the same dimensions as before but was in the shape of a conical helix surrounded by a paraboloidal reflector. The reaction vessel, through which the parallel light passed, was cylindrical, 2 cm. long and 7 cm. in diameter, and had quartz windows. Measurements of the percentage decomposition of 0·005M-oxalate in this cell were made, and then without changing the position, the decomposition of keten at 30 mm. pressure produced by a flash of the same energy was also measured. The extinction coefficients of keten under these conditions were measured between 2000 and

4000 Å by means of a Beckman spectrophotometer and are given in Fig. 3, since quantitative measurements for the gas do not appear in the literature. The energy distribution of the flash discharge between these wave-lengths, which is also required in the calculation, has been measured and is given elsewhere along with further details of the methods of actinometry (Christie and Porter, *loc. cit.*).

The results obtained, for two similar determinations with 30 mm. pressure of keten were: (1) oxalate decomposed = 5·30%, keten decomposed = 18·7%, ϕ_k = 6·8; (2) oxalate decomposed = 5·38%, keten decomposed = 17·6%, ϕ_k = 6·3.

No allowance is made for the change in absorption caused by the decomposition of keten; this and most other errors of the method are such as to make the above values of the quantum yield a minimum. It is therefore established that, even when the decomposition is only 18%,

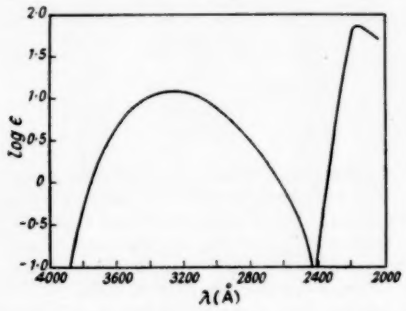


FIG. 3. *Extinction curve of keten gas: ε = decadic molar extinction coefficient (l. mole⁻¹ cm.⁻¹).*

the quantum yield is over 6, and we should expect that if higher decompositions could be obtained in this sytem even higher values of ϕ would be found.

DISCUSSION

The photolysis of keten at normal intensities has been shown to proceed by the following mechanism (Norrish, Crone, and Saltmarsh, *J.*, 1933, 1533; *J. Amer. Chem. Soc.*, 1934, **56**, 1644; Ross and Kistiakowsky, *ibid.*, p. 1112; Vanpee and Grard, *Ann. Mines Belg.*, 1950, **49**, 37; Kistiakowsky and Rosenberg, *J. Amer. Chem. Soc.*, 1950, **72**, 321):

$$CH_2{:}CO + h\nu = CH_2 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$2CH_2 = C_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$CH_2 + CH_2{:}CO = C_2H_4 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

It seems that the relative importance of reactions (2) and (3) depends on concentration, as might be expected, and, although the recent work quoted above supports reaction (3), the results of mirror experiments indicate that this reaction is accompanied by a considerable activation energy or steric factor (Pearson, Purcell, and Saigh, *J.*, 1938, 409; Norrish and Porter, *Discuss. Faraday Soc.*, 1947, **2**, 97).

Unless very high intensities are used, the effect of intensity on this reaction will simply be to alter the quantum yield, owing to competing reactions (2) and (3), but otherwise the mechanism and products remain unchanged. At very high intensities, such as those used in this investigation, several new possibilities arise.

(1) The concentration of intermediates may become comparable with that of the stable reactants or products. In the case of keten this is only an extreme case of the concentration effect considered above and cannot, by itself, produce any other effect than a reduction in the quantum yield if reactions (1), (2), and (3) only are considered.

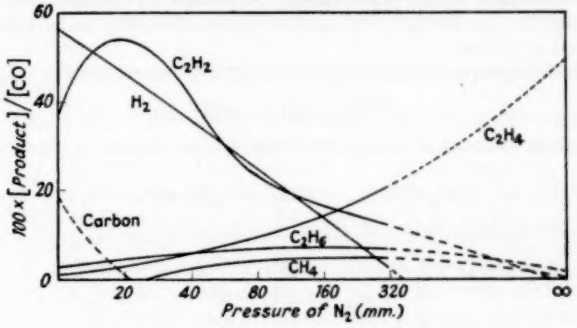
(2) The primary act may be changed by the simultaneous absorption of more than one quantum by the same molecule. The probability of this happening under the present experimental conditions is about 10^{-5} if each molecule absorbs, on an average, one quantum per flash. This is too small to make a significant contribution.

(3) Adiabatic reaction: the calculated time taken for the centre of a reaction vessel, 2 cm. in diameter and filled with nitrogen at 1 mm. pressure, to begin cooling is 0·3 millisec.,

and proportionately longer at higher pressures. As the duration of the flash is 1·5 millisec., the process will proceed nearly adiabatically for pressures greater than 10 mm. of mercury.

A cursory examination of the results in Tables 1, 2, and 3 suggests that the adiabatic effect, resulting in a rise in the temperature of the system, is playing a very important part. There are two ways in which the addition of an inert gas affects the kinetics of an ordinary photochemical reaction; first, it may act as a third body to facilitate recombination of atoms and radicals, and secondly, it may prevent diffusion of these bodies to the wall. These effects are insufficient in themselves to explain any of the observed phenomena, and a third effect, the increased thermal capacity of the system, must be invoked before it is possible to account for the effect of nitrogen in decreasing the quantum yield and restoring the products to those obtained at low intensity. The products are entirely as would be expected if a large temperature rise accompanies photolysis. The thermal decomposition of ethylene is known to give mainly acetylene and hydrogen as products, which is in accordance with our analysis at low nitrogen concentrations. The products from the runs 54—59, which were all carried out under the same conditions apart from the pressure of nitrogen, are plotted in Fig. 4 as a function of the nitrogen pressure, the concentrations being expressed as percentages of the carbon monoxide formed, which is equal to the

FIG. 4. *Products of photolysis of keten (expressed as percentage of carbon monoxide) as a function of nitrogen pressure. Original keten pressure = 10 mm. Hg.*



keten decomposed. Although the percentage decomposition is nearly 90 in each case, the products show a gradual transition from ethylene to its pyrolysis products as the nitrogen is decreased. An extrapolation to "infinite" nitrogen concentration, corresponding to zero temperature rise, will be expected to lead to the normal products of isothermal photolysis, as indicated. Similarly, at lower light intensity, comparison of the products in runs 30, 31, 32, 35, 34, and 46 shows the same effect and, in addition, a marked decrease in the amount of decomposition as the nitrogen is increased. If the reaction at high nitrogen dilution is to be identified with the normal photolysis, this implies that the quantum yield is greatly increased as the nitrogen is reduced and even if, in run 46, conditions are such that the "normal" quantum yield of unity is reached, in runs 30, 31, and 32 the quantum yield must be about 9.

The energy which is liberated as heat in a photochemical reaction arises in three ways: (1) Excess energy of the dissociation products; (2) degraded electronic energy; (3) heat of reaction of intermediates formed in the primary act. Too many values are uncertain, and too little is known about the mechanism at higher temperatures, to make an accurate estimate of the total heat liberated, but, for the purpose of discussion, a total figure of 100 kcal./g.-mol. of keten decomposed is probably of the right order. The resulting temperature rises, calculated for the series in Table 1, are as follows, it having been assumed that the decomposition at the highest dilution represents the true primary photochemical decomposition:

Run	30, 31, 32	35	34	46
Maximum temp.	800°	650°	500°	200°

In experiments such as 54 and 58, the effective specific heat is no longer that of nitrogen or keten, but is determined by the degree of dissociation. The temperature must be greatly in excess of that reached in the above experiments and is probably comparable with the temperature of hydrocarbon flames.

Studies of the pyrolysis of keten have been complicated by the rapid polymerisation to diketen and it is likely that, in the work of Akeroyd (*loc. cit.*) and Williamson (*J. Amer. Chem. Soc.*, 1934, **56**, 2216), who found respectively carbon dioxide and allene, and methane, as major products, the pyrolysis of diketen played an important part (Hurd and Williams, *ibid.*, 1936, **58**, 962). The nearest approach to our conditions was obtained by Muller and Peytral (*Compt. rend.*, 1933, **196**, 279) who pyrolysed keten in a flow system at 115°, in a platinum tube 2 mm. in diameter, the contact time being 2—3 millisec. They found as products: C_2H_4 21·8, C_2H_2 2·7, CO 63·9, CH_4 9·1, and H_2 2·5% as well as some carbon and polymer. Except for the absence of ethane, these are the same products as found by us.

We conclude, therefore, that comparisons with work on the thermal decomposition of keten under similar conditions, approximate estimations of the temperature rise, the nature of the products formed, the quantum-yield determinations and the effect of intensity, pressure, and especially the addition of inert gas, are all in accord with our explanation of the high-intensity reaction in terms of adiabatic heating. A more detailed consideration of the individual experiments, although it cannot lead to a complete elucidation of a mechanism as complex as this, shows that the main scheme of reactions may be represented as follows:

(*a*) Some radical disproportionation at relatively low temperatures, *e.g.*,

$$2CH_2 = CH_3 + CH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

followed by formation of small amounts of ethane and acetylene by recombination, and of methane by

$$CH_3 + C_2H_4 = CH_4 + C_2H_3, \text{ etc.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

(*b*) Radical-chain decomposition of keten, probably by

$$CH_3 + CH_2{:}CO = C_2H_5 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$C_2H_5 = C_2H_4 + H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$H + CH_2{:}CO = CH_3 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

giving quantum yields increasing with temperature, the activation energy of reaction (7) being 43 kcal. (Steacie, "Atomic and Free Radical Reactions," Reinhold, 1946, p. 96).

(*c*) Removal of methane by

$$CH_2 + CH_4 = C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

(*d*) Dehydrogenation of hydrocarbons by Rice–Herzfeld mechanisms:

$$C_2H_6 + H = C_2H_5 + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$C_2H_5 = C_2H_4 + H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$C_2H_4 + H = C_2H_3 + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

$$C_2H_3 = C_2H_2 + H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

(*e*) Decomposition of acetylene to carbon and hydrogen.

At higher temperatures the dehydrogenations may proceed directly without the radical chain, but, unless our temperature estimations are greatly in error, a radical-chain mechanism is necessary to explain the observed rate at lower temperatures.

The Mechanism of Carbon Formation.—Although many of the individual reactions given are better studied in other ways, the mechanism of carbon formation in the homogeneous gas phase is a problem which is inevitably associated with a complex set of experimental conditions, and the production of carbon by flash photolysis is a relatively simple one. It has the great advantage that the system may be heated homogeneously to a very high temperature, comparable with that obtained in flames, and then quenched

rapidly to room temperature. The products found, after heating to different temperatures, are therefore a valuable guide to the overall mechanism by which solid carbon is formed, and the system is entirely free from the heterogeneous complication introduced when the gas is heated by the wall of the vessel.

If solid carbon is formed, it is clear that polymerisation must occur at some stage, and most recent theories have been based on the postulate that the hydrocarbon first polymerises to large molecules, probably mainly aromatic ones, which are subsequently dehydrogenated. The analyses of the products in this work are quite contary to this theory. As the decomposition is increased and, consequently, a higher temperature attained, the products show a definite transition from ethane, *via* ethylene and acetylene, to solid carbon without the intermediate formation of any detectable amount of higher hydrocarbons. It is true that analyses of the solid always show some hydrogen present, but this is probably explained as polymerisation occurring at, or near to, the relatively cold wall. In all cases where this hydrogen could be estimated accurately, it was less than 1% of the total products and much less than the carbon or acetylene present. The important point is that, in spite of the rapid quenching, which results in the retention of an appreciable amount of all the intermediate products and keten, even when large amounts of carbon are formed, the amount of higher hydrocarbons formed is so small as to be undetectable in the gas phase. The experimental evidence supporting this statement is as follows :

(1) The carbon and hydrogen balances, especially at the higher decomposition when more accurate analyses were possible, show that the amount of hydrocarbons higher than C_2 must be very small.

(2) Combustion analyses on the hydrocarbon fractions corresponded to C_2 hydrocarbons to within 5%.

(3) Infra-red analysis of the products showed a just detectable amount of propylene present, corresponding to a very small fraction of the ethylene and acetylene.

(4) Ultra-violet spectroscopic examination of the products of many experiments showed aromatic hydrocarbons such as benzene, toluene, and naphthalene to be absent, the sensitivity of the test being such that less than 0·1 mm. would have been detectable.

In addition to this evidence, the analyses in runs (*e.g.*, 31, 32, 52, 53) where a large amount of carbon is formed show that nearly all the remaining hydrocarbon present is acetylene. This is also shown clearly in Fig. 4, where, although acetylene only is present in significant amounts at low nitrogen pressures, the carbon formation has just begun, with a consequent decrease in acetylene concentration. There can therefore be no doubt that acetylene is an essential intermediate in carbon formation from the more saturated hydrocarbons.

The detail of the last stage (*e*) of carbon formation from acetylene was avoided in the above reaction scheme, but we can now say, in view of these considerations, that it does not involve the formation of a *stable* higher hydrocarbon polymer. Two possibilities remain :

(1) Chain dehydrogenation of acetylene to C_2 radicals by the process

$$H + C_2H_2 = C_2H + H_2 \quad . . . . . \quad (14)$$

$$C_2H = C_2 + H \quad . . . . . \quad (15)$$

or perhaps direct thermal decomposition of acetylene to C_2 and hydrogen, followed in either case by polymerisation of C_2 radicals.

(2) A simultaneous polymerisation and dehydrogenation. This subject will be developed elsewhere in connection with other work on the reactions of acetylene and the chemistry of C_2. It is significant that the particle size in these experiments is within the range found in flames, and the high temperature and radical concentration, as well as the rate of the overall reaction, are very similar in the two cases. It seems probable that the reactions leading to carbon formation are not very different from those occuring in flames, the oxygen playing the same part as a free radical in the initial steps.

The Spectrum of Methylene.—As a result of the investigations reported here it became clear that, at high decompositions, the methylene-radical concentration would be low owing

to the high temperature and consequent high reaction rate. In the light of this information, further attempts to obtain its absorption spectrum have been made recently, the temperature rise being reduced by excess of nitrogen or carbon dioxide. If the lifetime of methylene under the conditions of the experiment was comparable with the duration of the flash, a concentration, estimated from the amount of decomposition, of several mm. of methylene would have been obtained. Nearly all the commonly occurring free-radical spectra have now been obtained by the method of flash spectroscopy (Porter, *loc. cit.*), and it is fairly certain that if methylene had a discrete absorption, corresponding to a fully allowed electronic transition, in the region between 2300 and 5000 Å it would have been detected with a methylene pressure of considerably less than 1 mm., the absorption path being 1 m. in length. In view of the long life of methylene found in mirror experiments in the presence of keten, it appears that methylene has no allowed transition to a stable electronic state in this region or, alternatively, that its association to ethylene occurs bimolecularly without the necessity of a third body and with a collision yield greater than 10^{-3}.

One of us (K. K.) is grateful to the Fulbright Commission for a Fellowship, during the tenure of which this work was carried out. We are also greatly indebted to Mr. J. K. Brown and Dr. J. W. Menter for the infra-red and electron-microscope measurements.

Department of Physical Chemistry,
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271. *Fission of Mixed Ethers by Boron Trichloride.*

By W. Gerrard and M. F. Lappert.

Fission of ethers by boron trichloride is rapid and entails the reaction $ROR' + BCl_3 \longrightarrow RCl + R'O{\cdot}BCl_2$. The distribution of the hydrocarbon group appears to be decided during the electrophilic attack of the trichloride on the ether and is in accordance with the influence of the degree of electron release on the reactivity of the two relevant carbon atoms. Thus *n*-butyl *sec.*-butyl ether appears as *sec.*-butyl chloride and *n*-butyl dichloroboronite, $BCl_2{\cdot}OBu^n$. Results are compared with those from ether fission by hydrogen iodide in which system anionic attack by iodine on the cation $ROR'H^+$ appears to decide the distribution. The above-mentioned ether then appears as *n*-butyl iodide and *sec.*-butyl alcohol in accordance with accepted principles.

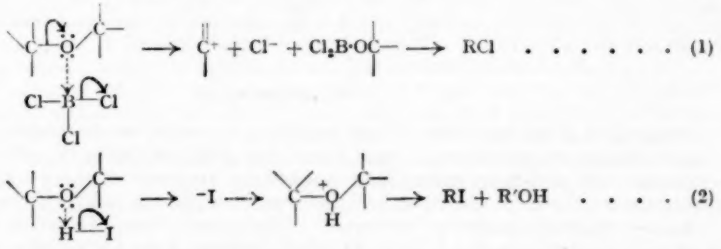
Ebelmen and Bouquet (*Ann. Chim. Phys.*, 1846, [iii], **17**, 54) observed a reaction between diethyl ether and boron trichloride, hydrogen chloride being evolved and ethyl "protoborate" formed. Similarly the methyl and *n*-pentyl "protoborates" were prepared. Gattermann (*Ber.*, 1889, **22**, 186) reported co-ordination compound between boron trichloride and diethyl ether. Ramser and Wiberg (*Ber.*, 1930, **63**, 1136) carried out reactions in an enclosed low-pressure apparatus and found that the trichloride and diethyl ether formed an addition compound, BCl_3,Et_2O, m. p. 56°, which on melting decomposed to ethyl dichloroboronite, $BCl_2{\cdot}OEt$, and ethyl chloride. This dichloroboronite reacted with a further molecule of ether to give the complex, $(BCl_2{\cdot}OR)_2,R_2O$, which was less stable than the trichloride–ether complex and disproportionated to the latter and diethyl chloroboronate, $BCl(OEt)_2$. The chloroboronate did not, however, react with more ether even at 100°.

We have shown (*J.*, 1951, 1020) that the interaction of boron trichloride with ethyl 1-methylheptyl ether and with ethyl 1-phenylethyl ether afforded ethyl dichloroboronite, and the chloride of the other group. The 2-chloro-octane was obtained with inversion but with considerable loss in rotatory power. The 1-chloro-1-phenylethane was completely racemised, but this was probably due to the racemisation of the chloride itself, by free boron trichloride.

In the present experiments, the ether (1 mol.) was added to the trichloride (1 mol.) at −80°. Separation was effected by fractional distillation at low temperatures with differential changes in pressures, and we relied on our knowledge of the stability and nature of the relevant dichloroboronites and chloroboronates (Gerrard and Lappert, *J.*, 1951, 2545). In order to study the fission of *sec.*-butyl *tert.*-butyl ether, the reactants were mixed in proportions, ether (2 mols.) and trichloride (1 mol.), because neither of the dichloroboronites is stable at room temperature. When the reactants were mixed in proportions 3 : 1, as in the case of the *n*-butyl *iso*butyl ether, the ether (1 mol.) was recovered unchanged. It might therefore be concluded that the chloroboronates do not react with ether. The chloroboronates were not isolated as their stability is low. The phenyl ethers (anisole and phenetole) with boron trichloride formed a white solid which was stable at −80°, but decomposed on melting when allowed to warm to 20°.

In no cases were dichloroboronites or alkyl halides from both the alkyl groups obtained by direct fission of the ether. In addition all the reactions appeared to have gone to completion. Experimental results are recorded in the Table, and are available for comparison with fission experiments with cold hydrogen iodide. Benton and Dillon (*J. Amer. Chem. Soc.*, 1942, **64**, 1128) treated with water the primary product from the interaction of ethers and boron tribromide, and obtained phenol and alkyl bromide from phenyl *iso*propyl and *n*-butyl phenyl ether. From benzyl *n*-propyl ether they got benzyl bromide and *n*-propyl alcohol.

The postulated mechanism for fission by boron trichloride is depicted in (1), whereas that for fission with hydrogen iodide is shown in (2) :



Fission of the C–O bond in the trichloride system will be favoured by electron accession to that carbon atom. In anisole, the phenyl group can cope with electron demand without materially weakening the nuclear C–O bond and therefore fission occurs by formation of the methyl cation. In the hydrogen iodide fission we do not expect protonisation of the oxygen normally to be sufficient to effect fission, so the process is visualised as an end-on (S_N2) anionic exchange (2). The halogen may therefore appear on that hydrocarbon group having the weaker electron release. Whereas boron trichloride fission of *n*-butyl *sec.*-butyl ether gives *sec.*-butyl chloride, it is *n*-butyl iodide which results in the hydrogen iodide system. With *iso*butyl *sec.*-butyl ether both reagents give *sec.*-butyl halide, presumably because the *iso*butyl structure offers a measure of steric hindrance in the S_N2 process, which is ineffective in the carbonium-cation mechanism of the boron trichloride reaction, which also leads to rearrangement of *iso*butyl to *tert.*-butyl radical. The formation of alkyl halide from phenyl alkyl ethers in both systems is in accord with the greater electron release by the alkyl group in mechanism (1) and its greater susceptibility to nucleophilic attack in mechanism (2).

The matter may be considered in terms of complex ions, $R^+[BCl_3{\cdot}OR']^-$ and $[R{-}\overset{H}{O}{-}R']^+I^-$. The complex anion could ionise unimolecularly (S_N1) to $R^+ + Cl^- + R'O{\cdot}BCl_2$; but which alkyl group separates as a cation during the formation of the anion will be determined by its relative electron-release capacity. The S_N2 attack of the iodine anion on the cation will also be in accord with known principles (Hughes and Ingold, cf. Hughes, *J.*, 1946, 968). Greenwood, Martin, and Emeléus (*J.*, 1950,

3030) concluded that the boron trifluoride–diethyl ether complex has the structure $(C_2H_5)^+[BF_3{\cdot}O{\cdot}C_2H_5]^-$. In the boron trichloride system distribution of hydrocarbon group would be decided during the formation of the corresponding complex *anion*, whereas in the hydrogen iodide system the decision is made during the S_N2 attack on the complex *cation*. Nevertheless the detailed career of the approaching molecules in the boron system is still somewhat elusive. Ramser and Wiberg's solid ether complex (*loc. cit.*) was stable up to the m. p. (56°), and with water gave back the ether. Whether the complex salt referred to could do this is a matter of opinion. Our solid compounds with anisole and phenetole were decomposed by water to give back the ether. We found no sign of such addition compounds with the other ethers.

Ether	Fission products (*a*) RCl	Fission products (*a*) RO·BCl_2	Fission products (*b*) Iodide	Fission products (*b*) ROH	Ref. (*b*)
Et, Pr^i	—	—	Et	Pr^i	Lippert (*Annalen*, 1893, **276**, 157).
Et, Bu^i	—	—	Et	Bu^i	,, ,, ,,
Bu^n, Bu^i	Bu^i + Bu^t	Bu^n	Bu^n	Bu^i	,, ,, ,,
Bu^n, Bu^s	Bu^s	Bu^n	Bu^n	Bu^s	,, ,, ,,
Bu^i, Bu^s	Bu^s	Bu^i	Bu^s	Bu^i	,, ,, ,,
Allyl, Pr^i	—	—	allyl	Pr^i	,, ,, ,,
Bu^n, Bu^t	Bu^t	Bu^n	—	—	—
Bu^i, Bu^t	Bu^t	Bu^i	—	—	—
Bu^s, Bu^t	Bu^t	Bu^s (borate)	—	—	—
Oct^n, Et	Oct^n	Et	—	—	—
Oct^s, Et	Oct^s	Et	—	—	—
PhEt, Et	PhEt	Et	—	—	—
Et, Pr^n	—	—	Et	Pr^n	Silva (*Ber.*, 1876, **8**, 1352).
Me, Et	—	—	Me	Et	,, ,,
Ph, Me	—	Ph	Me	Ph	Graebe (*Annalen*, 1866, **139**, 149).
Ph, Et	—	Ph	—	—	—

Experimental

Preparation of Ethers.—*iso*Butyl *tert.*-butyl and *sec.*-butyl *tert.*-butyl ether were prepared by Norris and Rigby's procedure (*J. Amer. Chem. Soc.*, 1932, **54**, 2088), the others by Williamson's synthesis. The *tert.*-butyl ethers were purified by thorough washing with water and final distillation from sodium, the others by treatment with phthalic anhydride to remove alcohol.

Fission of Ethers by Boron Trichloride.—*Ethyl* n-*octyl ether.* The ether (Found: C, 76·0; H, 13·9. Calc. for $C_{10}H_{22}O$: C, 75·9; H, 14·0%) (2·38 g., 1 mol.) was added to boron trichloride (3·4 g., >1 mol.) at −10°. The reaction was vigorous and a dark liquid remained. Direct distillation after 2 hours afforded ethyl dichloroboronite (1·7 g., 89%), b. p. 60—80° (redistilled), 78—80° (Found: Cl, 56·0; B, 8·34. Calc. for $C_2H_5OCl_2B$: Cl, 55·9; B, 8·5%), *n*-octyl chloride (1·8 g., 80%), b. p. 64—67°/10 mm. (redistilled), 58—60°/8 mm., $n_D^{18\cdot5}$ 1·4300 (Found: Cl, 23·8. Calc. for $C_8H_{17}Cl$: Cl, 23·9%), and a dark residue (0·55 g.). Unless otherwise stated, yields are expressed on: $ROR' + BCl_3 \longrightarrow RO{\cdot}BCl_2 + R'Cl$.

n-*Butyl* iso*butyl ether.* This ether (4·91 g., 1 mol.) was added to boron trichloride (4·44 g., 1 mol.) at −80°. The mixture was kept at 20° for 1½ hours. The reaction vessel was then cooled to −10° and was connected to the water-pump (20 mm.) for 3 hours. A liquid (3·4 g., 98%) consisting of a mixture of *tert.*- and *iso*-butyl chlorides, b. p. 50—65°, n_D^{20} 1·3880 (Found: as *tert.*-C_4H_9Cl, cold KOH hydrolysable Cl, 30·5; total Cl, 38·1. Calc. for C_4H_9Cl: Cl, 38·4%), had collected in a trap at −80°. At −10°/0·2 mm. crude *n*-butyl dichloroboronite (4·21 g., 73%) was collected (Found: Cl, 36·8; B, 6·0. Calc. for $C_4H_9OCl_2B$: Cl, 45·8; B, 7·0%). On two redistillations, the purer ester, b. p. 35—38°/12 mm. (Found: Cl, 45·0; B, 6·8%), was obtained. To show that this dichloroboronite was indeed the *n*-butyl ester, it was heated for 40 hours at 110°. On distillation, *n*-butyl chloride, b. p. 76—78°, n_D^{24} 1·3968, was obtained.

n-*Butyl* sec.-*butyl ether.* Boron trichloride (2·5 g., >1 mol.) was added to this ether (1·7 g., 1 mol.) at −10°. The mixture was sealed and set aside for 12 hours at 20°. Distillation afforded a mixture of *n*-butyl and *sec.*-butyl chlorides (2·2 g., 92%), b. p. 70—80° (which on treatment with water and redistillation had b. p. 70—77°, n_D^{20} 1·4012), and a residue (0·53 g.) containing boron trioxide (0·297 g., 96%) as shown by analysis. (Yields in this experiment were based on: $3ROR' + 2BCl_3 \longrightarrow 3RCl + 3R'Cl + B_2O_3$.) The mixture of halides obtained in the above experiment was thought to be formed by decomposition of an intermediate dichloroboronite caused by distillation at atmospheric pressure (Gerrard and Lappert, *loc. cit.*)

and so another sample of *n*-butyl *sec.*-butyl ether (4·0 g., 1 mol.) was added to boron trichloride (3·6 g., 1 mol.) at −80°. After 1 hour at −10°, the flask was evacuated (20 mm.) while at −10°, with a trap at −80°. After 2 hours, a liquid (2·48 g.), mainly *sec.*-butyl chloride (Calc. : 2·82 g.) but containing dissolved boron trichloride (15%) (Found : cold-water hydrolysable Cl, 13·7; B, 1·43%), was collected in the trap, and on treatment with moist lead carbonate afforded pure *sec.*-butyl chloride, b. p. 66—68°, n_D^{24} 1·3964. The remainder (4·80 g.) afforded, at 20°/0·5 mm., crude *n*-butyl dichloroboronite (4·4 g., 92%) (Found : Cl, 39·4; B, 6·1%) which on two redistillations afforded the pure compound, b. p. 38—39°/15 mm., n_D^{20} 1·4164 (Found : Cl, 45·0; B, 6·9%). On hydrolysis a portion (3·15 g.) gave *n*-butyl alcohol (1·12 g., 75%), b. p. 117°, n_D^{20} 1·4000. A residue (0·7 g.) remained from the primary distillation.

n-*Butyl* tert.-*butyl ether*. This ether (4·35 g., 1 mol.) was added to boron trichloride (3·89 g., 1 mol.) at −80°. After 1 hour at 20° the flask was cooled to −10°/20 mm. and a condensate (3·90 g.) was collected in a trap at −80°. On treatment with moist lead carbonate this afforded *tert.*-butyl chloride (2·50 g., 81%), b. p. 50—51°, n_D^{20} 1·3860 (Found : Cl, 38·0%). The remainder from the original distillation was crude *n*-butyl dichloroboronite (4·27 g., 82%) (Found : Cl, 39·0; B, 6·0%) which on two redistillations gave the pure ester, b. p. 38—40°/15 mm., n_D^{20} 1·3972 (Found : Cl, 45·2; B, 7·0%). The latter (1·5 g.) on hydrolysis gave *n*-butyl alcohol, b. p. 116°, n_D^{26} 1·3964.

iso*Butyl* sec.-*butyl ether*. The ether (3·27 g., 1 mol.) was added to boron trichloride (2·96 g., 1 mol.) at −80°. After 10 minutes at 20°, the flask was cooled to −10°/20 mm. and a condensate (1·91 g.) was collected at −80°. This was largely *sec.*-butyl chloride but contained boron trichloride (0·29 g.), as shown by chlorine and boron analysis in the cold. On treatment with moist lead carbonate the pure chloride, b. p. 68—70°, n_D^{21} 1·3957, was obtained. The remainder from the original distillation was further distilled at 0·5 mm., and crude *iso*butyl dichloroboronite (3·90 g.; Calc., 3·90 g.) (Found : Cl, 38·7; B, 6·0%) was obtained; this, purified by two distillations, had b. p. 32—34°/20 mm., n_D^{20} 1·4087, d_4^{20} 1·042 (Found : Cl, 45·1; B, 6·9%). A portion on aqueous treatment yielded *iso*butyl alcohol, b. p. 105—106°, n_D^{21} 1·4148.

iso*Butyl* tert.-*butyl ether*. This ether (4·00 g., 1 mol.) was added to boron trichloride (3·60 g., 1 mol.) at −80°. Evacuation (20 mm.) of the reaction vessel at 0° gave crude *tert.*-butyl chloride (3·0 g.) which was condensed at −80° and, when treated with moist lead carbonate, yielded the pure chloride (2·3 g., 80%), b. p. 50—51°, n_D^{21} 1·3852 [Found : Cl (cold KOH hydrolysable), 38·2%]. The residue from the primary distillation was crude *iso*butyl dichloroboronite (4·87 g.; Calc., 4·76 g.) (Found : Cl, 37·5; B, 7·0%) which on two redistillations afforded the pure ester, b. p. 32—33°/19 mm., n_D^{21} 1·4090 (Found : Cl, 45·1; B, 7·1%).

Interaction of Boron Trichloride (1 *mol.*) *and* n-*Butyl* iso*Butyl Ether* (3 *mols.*).—*n*-Butyl *iso*butyl ether (9·14 g., 3 mols.) was added to boron trichloride (2·75 g., 1 mol.) at −80°. The mixture was kept for 1 hour at 20°. Distillation afforded a liquid (6·1 g.), b. p. 55—85°, which was probably a mixture of *tert.*-, *n*-, and *iso*-butyl chlorides (Calc., 6·46 g.), a second fraction [unchanged ether (2·5 g.; Calc., 3·05 g.)], b. p. 25—35°/20 mm., n_D^{25} 1·3950 (Found : Cl, 0%), and a final fraction of tri-*n*-butyl borate (1·65 g., 92%), b. p. 71°/0·5 mm. (redistilled), 105—106°/10 mm., n_D^{25} 1·4030 (Found : B, 4·8. Calc. for $C_{12}H_{27}O_3B$: B, 4·7%). This borate on hydrolysis gave *n*-butyl alcohol, b. p. 117°, n_D^{20} 1·3993. A residue (0·60 g.) remained from the primary distillation, containing boron trioxide (0·551 g.; Calc., 0·545 g.) as shown by analysis. The chloride fraction was shaken with moist lead carbonate and fractionated, giving (i) (2·0 g.) b. p. 53—64°, n_D^{25} 1·3855 (Found : Cl, as *tert.*-C_4H_9Cl, 21·4; total Cl, 38·2%), (ii) (3·0 g.) b. p. 64—69°, n_D^{25} 1·3910 (Found : Cl, as *tert.*-C_4H_9Cl, 15·3; total Cl, 38·4%), and (iii) (0·91 g.) b. p. 69—78°, n_D^{25} 1·3917 (Found : Cl, as *tert.*-C_4H_9Cl, 0·87; total Cl, 37·9%).

The *tert.*-butyl chloride was estimated by hydrolysis in cold aqueous potassium hydroxide, and the total chloride was found by hydrolysis in hot alcoholic potassium hydroxide in a sealed tube. Yields in the above experiment are based on : $3ROR' + BCl_3 \longrightarrow ROR'$ (unchanged) $+ (RO)_2BCl + R'Cl$; $3(RO)_2BCl \longrightarrow (RO)_3B + 3RCl + B_2O_3$.

Interaction of Boron Trichloride (1 *mol.*) *and* sec.-*Butyl* tert.-*Butyl Ether* (2 *mols.*).—*sec.*-Butyl *tert.*-butyl ether (3·54 g., 2 mols.) was added to boron trichloride (1·60 g., 1 mol.) at −80°. After 1½ hours at 20°, the mixture was kept at 20°/20 mm. A liquid (3·70 g.; Calc., 3·75 g.) consisting probably of a mixture of *tert.*- and *sec.*-butyl chlorides was condensed at −80°. After shaking with moist lead carbonate and redistillation, this mixture had b. p. 51—67°, n_D^{20} 1·3929 (Found : Cl, as *tert.*-C_4H_9Cl, 23·2; total Cl, 38·2%). The remainder of the original distillation gave tri-*sec.*-butyl borate (0·91 g., 87%), b. p. 82°/10 mm., n_D^{20} 1·3970 (Found : B, 4·8%), and a residue (0·51 g.) containing boron trioxide (0·33 g.; Calc., 0·317 g.) as shown by analysis. The tributyl borate on hydrolysis gave *sec.*-butyl alcohol, which was

immiscible in water (contrast *tert.*-butyl alcohol). Yields in this experiment are based on: $2ROR' + BCl_3 \longrightarrow (RO)_2BCl + R'Cl$; $3(RO)_2BCl \longrightarrow (RO)_3B + 3RCl + B_2O_3$.

Interaction of Boron Trichloride (1 *mol.*) *and Anisole* (1 *mol.*).—Anisole (4·50 g., 1 mol.) was added to boron trichloride (4·90 g., 1 mol.) at −80°. A white solid formed instantly, but this slowly melted when allowed to warm to room temperature and gave a purple, clear liquid. The mixture was kept at 20°/20 mm. for 40 minutes. The remainder (6·55 g.; *i.e.*, loss in weight, 2·85 g.; Calc. loss for CH_3Cl only, 2·12 g.) was phenyl dichloroboronite and the products [diphenyl chloroboronate and triphenyl borate (boron trichloride being also removed at the pump)] of its apparent disproportionation $2RO{\cdot}BCl_2 \longrightarrow (RO)_2BCl + BCl_3$; $3(RO)_2BCl \longrightarrow 2(RO)_3B + BCl_3$ [Found: Cl (cold water hydrolysable) 31·2; B, 4·8. $C_6H_5OBCl_2$ requires Cl, 40·1; B, 6·3%]. Distillation afforded a forerun (1·3 g.), b. p. 30—65°/0·2 mm. (Found: Cl, 27·0; B, 5·7%), and a solid (triphenyl borate) (3·5 g.) (Calc., 4·5 g. for complete disproportionation), b. p. 160—170°/0·2 mm. (Found: B, 3·9. Calc. for $C_{18}H_{15}O_3B$: B, 3·8%).

Interaction of Boron Trichloride (1 *mol.*) *and Phenetole* (1 *mol.*).—Phenetole (3·85 g., 1 mol.) was added to boron trichloride (3·7 g., 1 mol.) at −80°. A white solid formed. This solid, as the corresponding one in the preceding experiment with anisole, may be the boron trichloride–ether complex, which decomposes on melting. The mixture which was purple was kept for 15 hours at 20°. Free boron trichloride was then present. The mixture was kept at 15 mm. and a residue (3·34 g.) (loss in weight, 4·21 g.; Calc. loss in weight due to C_2H_5Cl and remainder of Cl as BCl_3, 4·51 g.), which on distillation afforded a forerun (1·04 g.) of diphenyl chloroboronate and triphenyl borate, b. p. 120—150°/0·2 mm. (Found: Cl, 7·6; B, 4·3%), and triphenyl borate (2·3 g.; total triphenyl borate, 3·04 g., for complete disproportionation), b. p. 178°/0·4 mm. (Found: B, 3·8%).

Addition of water to the white solid formed at −80° (25 minutes after its formation) showed that no alkyl chloride had been formed (Found: Cl, 43·9; B, 4·4. $C_8H_{10}OCl_3B$ requires Cl, 44·5; B, 4·5%); unchanged phenetole, b. p. 170°, n_D^{19} 1·5083, was obtained. Similarly the anisole–boron trichloride *complex* with water (Found: Cl, 47·0; B, 4·7. $C_7H_8OCl_3B$ requires Cl, 47·4; B, 4·8%) gave the ether, b. p. 154°, n_D^{19} 1·5182.

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272. N-*Substituted Glycosylamines. Part II.** *The Influence of Water on the Preparation of* N-*Arylglycosylamines.*†

By G. P. ELLIS and JOHN HONEYMAN.

The reaction of D-ribose with aniline has been investigated and the influence of water established in deciding which isomer is obtained. This result has been applied generally to the reaction of monosaccharides with primary aromatic amines, with the consequent preparation of new compounds. A general method for preparing a number of *N*-*p*-tolylaldosylamines is described: possible uses include the identification of aldoses. The ultraviolet absorption of some of the compounds in methanol has been measured: no change in absorption was observed during mutarotation.

THE condensation of D-ribose with aniline was studied by Berger and Lee (*J. Org. Chem.*, 1946, **11**, 75), who obtained two isomers which they called aniline-*N*-D-ribofuranoside, formed when the reaction was carried out in boiling ethanol, and aniline-*N*-D-ribopyranoside, formed by condensation in aqueous ethanol at room temperature. The pyranoside was converted into the furanoside by heating it under reflux in ethanol for an hour or by leaving it in ethanol at room temperature. According to the nomenclature now being adopted these compounds are *N*-phenyl-D-ribofuranosylamine and *N*-phenyl-D-ribopyranosylamine respectively.

* Part I, *J.*, 1950, 967.

† Named arylamine-*N*-glycosides in Part I.

The evidence presented by Berger and Lee (*loc. cit.*) for assigning the furanose and pyranose structures to the isomers was critically reviewed by Honeyman and Tatchell (*J.*, 1950, 967), who pointed out that characterization of the isomers was incomplete. Because of the uncertainty of the structures the isomer previously considered to be *N*-phenylribofuranosylamine will now be called *A*, and that thought to be the pyranosylamine *B*.

Much of Berger and Lee's work on the substituted ribosylamines was repeated by Howard, Kenner, Lythgoe, and Todd (*J.*, 1946, 855), who confirmed most of the American workers' findings. They showed, however, that the conversion of *B* into *A* in refluxing ethanol did not always take place. In some cases no conversion at all took place, whereas in others, under apparently the same experimental conditions, some or all of *B* was converted into *A*.

The work described in this paper clarifies the conditions which govern the formation and interconversion of the two *N*-phenylribosylamines, and expands the previous communication on this subject (Ellis and Honeyman, *Nature*, 1951, **167**, 239). Experiments on the condensation of D-ribose with aniline at various temperatures and in various solvents showed that, contrary to the suggestions of previous workers, temperature was not an important influence on the nature of the isomer produced. Thus, *B* was produced in aqueous ethanol at room temperature or at the boiling point. Further, the presence of moisture invariably resulted in the production of *B*, whereas *A* was obtained only in anhydrous ethanol. Similarly, even a small amount of water prevented conversion of *B* into *A* in boiling ethanol; this probably explains why Howard *et al.* (*loc. cit.*) did not obtain consistent results. Conversely, a solution of *A* in aqueous ethanol, whether refluxed or not, deposits crystals of *B*. The importance of water in the formation of the *N*-phenylribosylamines was shown conclusively by two experiments. The sugar and amine were boiled in anhydrous ethanol with the exclusion of moisture and the hot reaction mixture divided into three parts. In the first vessel, which was immediately stoppered and cooled, crystals of *A* separated. A small amount of water was added to the other two parts. One was cooled immediately and the other boiled for 15 minutes more: both deposited crystals of *B*. In another experiment, the components were heated under reflux in aqueous ethanol and the reaction mixture was divided into two parts. One part was seeded with *B* and the other with *A*, but *B* separated from both. The specific rotations of the two isomers in methanol (which had not been reported at the time this work was done, but which have since been published by Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433) showed a change in rotation in the same direction to approximately the same end-point: *A*, $[\alpha]_D^{20}$ +134·9° ⟶ +14·1° (*c*, 0·4 in methanol); *B*, $[\alpha]_D^{14}$ +23·8° ⟶ +8·3° (*c*, 0·4 in methanol). No mutarotation was observed in pyridine, even on addition of a drop of water. This is in contrast to observations by Berger and Lee, Howard *et al.*, and Butler *et al.*, who record mutarotation in pyridine or moist pyridine. It was largely on the basis of the mutarotation that Berger and Lee (*loc. cit.*) considered that the isomers had different rings. Certainly it is clear that mutarotation involves the production of at least a third compound, but no evidence has been obtained so far as to its nature. Evaporation of the solutions after equilibration resulted in the separation of *B*.

A similar cycle of reactions was carried out with *p*-toluidine and D-ribose. Berger and Lee (*J. Org. Chem.*, 1946, **11**, 84) describe the only known *N*-*p*-tolylribosylamine, m. p. 102—103° (decomp.), $[\alpha]_D^{27\cdot5}$ +53·2° (in pyridine), prepared at room temperature in ethanol containing a trace of water, as a white powder containing two molecules of ethanol. In the present work, *N*-*p*-tolylribosylamine, m. p. 123° (decomp.), $[\alpha]_D^{18}$ +58·6° (in pyridine), separated from aqueous ethanol at room temperature as a crystalline hemihydrate. This corresponds with the *N*-phenylribosylamine *B* obtained by a similar method and is called isomer *B*. When D-ribose was heated with *p*-toluidine in anhydrous ethanol an isomer (*A*), m. p. 130° (decomp.), $[\alpha]_D^{17}$ +178·2° ⟶ +76·0° (in pyridine), was obtained. The conditions of formation and interconversion of these two isomers followed those of the *N*-phenylribosylamines exactly. The change of rotation of their methanol solutions is also analogous, *viz.*: *A*, $[\alpha]_D^{20}$ +136·2° ⟶ +12·5°; *B*, $[\alpha]_D^{18}$ +22·1° ⟶ +11·7°. *A* showed mutarotation in dry pyridine but *B* did not.

Berger and Lee (*loc. cit.*, p. 84) prepared *N*-*o*-nitrophenyl-D-ribosylamine, m. p. 183—185° (decomp.), $[\alpha]_D^{28}$ −109° (in pyridine), by reaction at room temperature in aqueous ethanol. We have obtained the same compound *B* under these conditions and a new isomer *A*, m. p. 167—168° (slight decomp.), $[\alpha]_D^{20}$ −122·5° (in pyridine), by reaction in boiling anhydrous ethanol. The specific rotations of these isomers are more similar than in the previous cases, but *A*, $[\alpha]_D$ −122°, was consistently obtained from refluxing anhydrous ethanol and was converted into *B*, $[\alpha]_D$ −109°, by recrystallization from aqueous ethanol. The compounds were also more stable than other substituted ribosylamines and have remained as yellow needles with no signs of decomposition on normal storage for several months. The evidence points strongly to the existence of two isomers, as for the others reported above. Howard *et al.* (*loc. cit.*) mention, without experimental details, that only one *N*-*o*-nitrophenylribosylamine was obtained from condensation by the two methods described by Berger and Lee.

In view of the important role of moisture in the preparation of *N*-substituted ribosylamines, the investigation was extended to other sugars. The reaction of glucose and galactose with *p*-toluidine under anhydrous conditions was found to give new isomers. Similarly, with glucose and aniline, a dextrorotatory isomer was obtained, but the product of several reactions did not have such a consistent specific rotation as did the *N*-*p*-tolylglucosylamine. The amorphous nature of *N*-phenylglucosylamine, no matter how obtained, is a complicating factor in this instance. In the same way a different *N*-phenyl-D-galactosylamine was obtained. Attempts to recrystallize the new galactose and glucose derivatives under anhydrous conditions were not very successful, as some isomerization usually occurred. However, the same *N*-phenyl- or *N*-*p*-tolyl-D-xylosylamine was obtained by both methods of condensation.

In the majority of cases where two different isomers were prepared, the final value of the specific rotation was the same for both isomers. However, the facile conclusion that the two isomers are anomers is unjustified if the case of *N*-phenylribosylamines is borne in mind.

The ultra-violet light absorption of *N*-phenyl-D-mannosylamine and of both isomers *A* and *B* of *N*-*p*-tolylribosylamine was measured. Kuhn and Dansi (*Ber.*, 1936, **69**, 1745) recorded the ultra-violet light absorption of *N*-*p*-tolylglucosylamine in ethanol. In the present work, the absorption was measured in methanol for a number of days at the same time as the mutarotation was being observed polarimetrically. There was no appreciable change in the absorption corresponding to the change in specific rotation which took place simultaneously. In this connexion, it is interesting that the absorption curve for the *N*-substituted glycosylamines closely resemble those of the simple aromatic amines, the main difference being that the maxima are moved laterally to a slight extent. For *N*-phenyl-D-mannosylamine the maxima are at 2400 (log ε 4·48) and 2850 Å (log ε 3·52) : *N*-*p*-tolylribosylamine *A* has $\lambda_{max.}$ 2450 (log ε 4·47) and 2900 Å (log ε 3·72) ; *N*-*p*-tolylribosylamine *B* showed $\lambda_{max.}$ 2500 (log ε 5·62) and 2940 Å (log ε 4·25). Aniline is reported (for references see *Ann. Reports*, 1945, **42**, 124) to have $\lambda_{max.}$ 2300 (log ε 3·90) and 2800 Å (log ε 2·30).

Physical constants of N-aryglycosylamines obtained by present authors.

	Isomer A		Isomer B	
	M. p.	$[\alpha]_D$ *	M. p.	$[\alpha]_D$ *
N-Phenylribosylamine	133—134°	+134·9° ⟶ +14·1°	112—114°	+24·3° ⟶ +9·4°
N-*p*-Tolylribosylamine	130	+136·2 ⟶ +12·5	123	+22·1 ⟶ +11·7
N-*o*-Nitrophenylribosylamine	167—168	− 122·5 †	193—194	−109·1 †
N-Phenylglucosylamine	134—135	+53 ⟶ −20·6	—	+10 ⟶ −52
N-*p*-Tolylglucosylamine	135—136	+209 ⟶ −45	117—118	−101 ⟶ −46
N-Phenylgalactosylamine ...	141—143	−22·1 ⟶ −40·3	157—158	−92 ⟶ −43·5
N-*p*-Tolylgalactosylamine ...	—	−33·0 ⟶ −14·1	161—162	−80 ⟶ +8·8

* In methanol, unless specified. † In pyridine.

The ease of reaction of amines with sugars in aqueous ethanol at room temperature, and the purity and frequent excellent crystalline form of the product, suggested the possible

development of a method for the characterization of sugars (see Table). The products obtained in this way are thought to be the same as those prepared by a different method by Weygand (*Ber.*, 1939, **72**, 1663), although this worker does not always record specific rotations of his products and melting points are not very reliable. The method described is preferred to Weygand's because, generally, the yield and purity were better and recrystallization was unnecessary. The chief disadvantage of these derivatives for characterization purposes is the impossibility of storing them for long without decomposition, but acetylation as described by Honeyman and Tatchell, Butler *et al.*, and others, gives very easily a more desirable product with sharp melting point, characteristic specific rotation without mutarotation, and excellent stability. An attempt was made to evolve a general procedure using one amine, which would condense with a number of sugars under these conditions. The most suitable tried was *p*-toluidine, which reacted readily (with standardized quantities) in aqueous ethanol at room temperature, to give a crystalline *N*-*p*-tolylglycosylamine with the following sugars: D-ribose, D-mannose, D-galactose, D-glucose, and, less successfully, D-xylose. The crystals which separated were filtered off, washed with ethanol and with ether until free from amine, and dried in a vacuum. With L-arabinose crystalline material was extremely difficult to obtain, even on removal of some of the solvent, owing to the solubility of the product. The ketoses tried, D-fructose and D-sorbose, did not react with *p*-toluidine under these conditions. The method has possibilities for separating certain aldoses from ketoses. With mannose and ribose, the separation of crystalline material was rapid and the final yield was high.

Experimental

Solvents used in the determination of specific rotations were purified and freed from water. The initial $[\alpha]_D$ stated was obtained, where necessary, by extrapolation to zero time: the final value is the equilibrium one. M. p.s, which are uncorrected, were somewhat variable; melting was accompanied by decomposition.

The crystalline products were purified by washing them with ethanol and with ether and were dried in a vacuum desiccator.

N-Phenyl-D-ribosylamine A.—D-Ribose (0·4 g., 1 mol.) was dried for 2 hours at 75° and placed in a dry flask containing magnesium-dried ethanol (4 ml.). Freshly redistilled aniline (0·3 g., 1·2 mols.) was added and the mixture boiled for 2 hours under a dried condenser carrying a calcium chloride tube. The flask was then stoppered and cooled. The solution deposited crystals (0·4 g., 67%) of *N*-phenyl-D-ribosylamine *A*, m. p. 133—134°, $[\alpha]_D^{20}$ +176·4° (*c*, 0·8 in pyridine), +134·9° ⟶ +14·1° (after 12 days) (*c*, 0·4 in methanol), $[\alpha]_D^{16}$ +172·1° ⟶ +37·2° (*c*, 0·2 in ethanol).

N-Phenylribosylamine B.—Prepared by Berger and Lee's method (*loc. cit.*), *N*-phenylribosylamine *B* was obtained as white needle-shaped crystals (93%), m. p. 112—114°, $[\alpha]_D^{20}$ +60·2° (*c*, 1·0 in pyridine), $[\alpha]_D^{14}$ +23·8° ⟶ +8·3° (*c*, 0·4 in methanol).

Recovery of N-*Phenylribosylamine* B *from Methanolic Solutions.*—(i) The methanolic solution used for determination of the specific rotation of *A* was allowed to evaporate at room temperature in the laboratory atmosphere. It gave crystals of *B*, m. p. 112—115°, $[\alpha]_D^{15}$ +62·2° (*c*, 1·0 in pyridine), +24·0° ⟶ +9·9° (*c*, 0·7 in methanol).

(ii) A methanolic solution of *B* was left in a stoppered flask until its specific rotation had reached a constant value. It was then allowed to evaporate slowly at room temperature and gave crystals of *B*, m. p. 114—116°, $[\alpha]_D^{16}$ +60·4° (*c*, 0·7 in pyridine), +24·3° ⟶ +9·4° (*c*, 0·6 in methanol).

Conversion of N-*Phenylribosylamine* A *into* B.—A sample of *A* (1 g.) was added to absolute ethanol (5 ml.) and water (10 ml.). After being refluxed for 10 minutes it was left at room temperature overnight. The solution deposited crystals of *B*, $[\alpha]_D^{17}$ +62·2° (*c*, 1·0 in pyridine).

Conversion of N-*Phenylribosylamine* B *into* A.—(i) A solution of *B* (1 g.) in magnesium-dried ethanol (8 ml.) was refluxed in dried apparatus in the absence of moisture for 1 hour. The flask was then stoppered and cooled. The solution deposited crystals of *A*, $[\alpha]_D^{15}$ +186·2° (*c*, 0·8 in pyridine), $[\alpha]_D^{16}$ +153·8° ⟶ +14·2° (*c*, 0·4 in methanol).

(ii) A solution of *N*-phenylribosylamine *B* (3 g.) in anhydrous ethanol (24 ml.) was refluxed under anhydrous conditions for 1 hour and then divided into three portions. The first was immediately stoppered and left to cool, whereupon it deposited crystals of *A*, m. p. 132—

134°, $[\alpha]_D^{17}$ +176·4° (*c*, 1·0 in pyridine). The second was left to cool after one drop of water had been added to it. This gave crystals of *B*, $[\alpha]_D^{17}$ +59·8° (*c*, 0·8 in pyridine). The third was refluxed for 15 minutes with two drops of water. On cooling, it deposited crystals of *B*, $[\alpha]_D^{17}$ +60·1° (*c*, 0·9 in pyridine).

Physical Constants of N-*Phenylribosylamines.*—The physical constants of the *N*-phenylribosylamines, together with those given by other workers, are tabulated below :

Reference (*locc. cit.*)	*A*, m. p.	*A*, $[\alpha]_D$ in methanol	*A*, $[\alpha]_D$ in pyridine	*B*, m. p.	*B*, $[\alpha]_D$ in methanol	*B*, $[\alpha]_D$ in pyridine
Present authors	133—134°	+134·9° ⟶ +14·1°	+176·4°	112—114°	+23·8° ⟶ +8·3°	+60·2°
Berger and Lee	138—140	—	+176·5 ⟶ +156·6	125—127	—	+63·4 ⟶ +48·6
Butler *et al.* ...	123—124	+135 ⟶ +12	+182 ⟶ +52·3	114—116	+23 ⟶ +13	+62 ⟶ +50
Howard *et al.* ...	126—127	—	+180 (dry solvent) +180 ⟶ +161 (moist solvent)	119	—	+60 (dry slovent) +60 ⟶ +48·4 (moist solvent)

N-p-*Tolyl*-D-*ribosylamine* A.—(i) D-Ribose (0·5 g., 1 mol.) was dried at 75° for 2 hours and dissolved in freshly dried ethanol (4 ml.). After addition of *p*-toluidine (0·35 g., 1 mol.) the solution was refluxed for 2 hours with exclusion of moisture. The flask was immediately stoppered and on cooling deposited N-p-*tolyl*-D-*ribosylamine* A, m. p. 130°, $[\alpha]_D^{20}$ +136·2° ⟶ +12·5° (*c*, 0·3 in methanol), $[\alpha]_D^{17}$ +178·2° ⟶ +76·0° (*c*, 0·3 in dry pyridine) (Found : C, 60·3; H, 6·9; N, 6·0. $C_{12}H_{17}O_4N$ requires C, 60·3; H, 7·1; N, 5·9%).

N-p-*Tolylribosylamine* B.—(i) (cf. Berger and Lee, *loc. cit.*, p. 84). To D-ribose (2 g., 1 mol.) in 0·001N-sulphuric acid (5·5 ml.), *p*-toluidine (2 g., 1·5 mols.) in ethanol (10 ml.) was added. The white needles (3·0 g., 94%) which separated after 20 hours at room temperature and 5 hours at 0° were found to be N-p-*tolyl*-D-*ribosylamine* B, m. p. 123°, $[\alpha]_D^{18}$ +58·6° (*c*, 1·0 in pyridine), $[\alpha]_D^{18}$ +22·1° ⟶ +11·7° (*c*, 0·4 in methanol) (Found : C, 58·1; H, 7·3; N, 5·8%. $C_{12}H_{17}O_4N,\frac{1}{2}H_2O$ requires C, 58·1; H, 7·3; N, 5·6%). Berger and Lee (*loc. cit.*) describe *N*-*p*-tolyl-D-ribosylamine, m. p. 102—103°, $[\alpha]_D^{27\cdot5}$ +53·2° (*c*, 2·0 in pyridine) as a white powder, analysis indicating the presence of two molecules of ethanol.

(ii) The product present in a solution obtained by heating D-ribose (0·5 g., 1 mol.) with *p*-toluidine (0·38 g., 1·2 mols.) in anhydrous ethanol for 2 hours was refluxed for 5 minutes more after addition of two drops of water. On purification it gave crystals of *B*, $[\alpha]_D^{18}$ +65° (*c*, 0·3 in pyridine), $[\alpha]_D^{18}$ +22·6° ⟶ +12·7° (*c*, 0·4 in methanol).

(iii) A mixture of D-ribose (0·5 g., 1 mol.), *p*-toluidine (0·4 g., 1·3 mols.), and water (0·3 ml.) was heated together on a steam-bath for 5 minutes after the solution became homogeneous. On cooling, ethanol (2 ml.) was added, whereupon it gave *N*-*p*-tolylribosylamine *B* (0·6 g., 75%), m. p. 123—124°, $[\alpha]_D^{18}$ +60·2° (*c*, 0·7 in pyridine).

Conversion of N-p-*Tolylribosylamine* B *into* A.—A solution of *N*-*p*-tolylribosylamine *B* (0·3 g.) in anhydrous ethanol (3 ml.) was refluxed in previously dried apparatus with exclusion of moisture for 1 hour. The flask was stoppered and cooled, whereupon the solution gave *A*, m. p. 129—130°, $[\alpha]_D^{19}$ +127·6° ⟶ +11·7° (after 24 hours) (*c*, 0·2 in methanol).

N-o-*Nitrophenyl*-D-*ribosylamine* B (cf. Berger and Lee, *loc. cit.*, p. 84).—D-Ribose (0·5 g., 1 mol.) in 0·001N-sulphuric acid (1 ml.) was added to *o*-nitroaniline (0·7 g., 1·5 mols.) in ethanol (2 ml.). The amine dissolved as the reaction proceeded at room temperature. After 30 days, the solution deposited yellow anhydrous crystals (0·8 g., 89%) of *N*-*o*-nitrophenylribosylamine, m. p. 193—194°, $[\alpha]_D^{20}$ −109·1° (*c*, 0·3 in pyridine). This is provisionally called *B*, and was prepared by Berger and Lee (*loc. cit.*), who give m. p. 183—185°, $[\alpha]_D^{28}$ −109° (*c*, 1·0 in pyridine).

N-*o*-*Nitrophenyl*-D-*ribosylamine* A.—(i) A suspension of D-ribose (1 g., 1 mol.), ammonium chloride (0·05 g.), and *o*-nitroaniline (0·96 g., 1·1 mols.) was heated under reflux in anhydrous ethanol (5 ml.) for 2 hours with exclusion of moisture. The flask was then stoppered and placed in the refrigerator. This produced orange-yellow crystals (1·7 g., 94%) of N-o-*nitrophenyl*-D-*ribosylamine* A, m. p. 167—168°, $[\alpha]_D^{20}$ −122·5° (*c*, 0·2 in pyridine) (Found : C, 49·3; H, 5·0. $C_{11}H_{14}O_6N_2$ requires C, 48·9; H, 5·2%).

(ii) A solution of *B* (0·5 g.) was refluxed for 2 hours in anhydrous ethanol (12 ml.) with

careful exclusion of moisture. The crystals which separated were *A*, m. p. 192—193°, $[\alpha]_D^{17}$ −123·9° (*c*, 0·2 in pyridine).

Conversion of N-o-*Nitrophenylribosylamine* A *into* B.—Isomer *A* (0·5 g.) was heated for 2 hours in 90% aqueous ethanol (12 ml.). On cooling, the solution deposited yellow crystals of *B*, m. p. 192—193°, $[\alpha]_D^{19}$ −108·2° (*c*, 0·3 in pyridine).

The solubility of both *N*-*o*-nitrophenylribosylamines in methanol and in ethanol was too low for optical observations to be made.

N-*Phenyl*-D-*xylosylamine*.—Dry D-xylose (2 g., 1 mol.) and redistilled aniline (2 ml., 1·6 mols.) were refluxed in anhydrous ethanol (12 ml.) for 1½ hours. The pale yellow solution was divided into two portions. One was stoppered and allowed to cool. White needles of *N*-phenylxylosylamine, m. p. 144—145°, $[\alpha]_D^{21}$ −82·1° ⟶ −21·6° (*c*, 0·6 in methanol), separated. Two drops of water were added to the other and the solution was refluxed for 5 minutes more. On cooling, it deposited crystals of the same xylosylamine, m. p. 143—144°, $[\alpha]_D^{20}$ −84·1° ⟶ −21·9° (*c*, 0·8 in methanol). Weygand (*loc. cit.*) gives m. p. 140—141°. Butler *et al.* (*loc. cit.*) give m. p. 142—144°, $[\alpha]_D^{19}$ −90° ⟶ −48° (*c*, 1·0 in methanol).

N-p-*Tolyl*-D-*xylosylamine*.—(i) Dry D-xylose (2 g., 1 mol.) and *p*-toluidine (2 g., 1·6 mols.) were heated under reflux in anhydrous ethanol (12 ml.) for 2 hours with the exclusion of moisture. The light brown solution on cooling deposited *N*-*p*-tolylxylosylamine (2·4 g., 74%), m. p. 124—125°, $[\alpha]_D^{20}$ −76·6° ⟶ −21·2° (*c*, 0·4 in methanol).

(ii) D-Xylose (2 g., 1 mol.) and *p*-toluidine (1·6 g., 1·3 mols.) were heated in water (0·6 ml.) according to Weygand's method (*loc. cit.*). The product had m. p. 124—125°, $[\alpha]_D^{14}$ −59·0° (*c*, 0·5 in pyridine), $[\alpha]_D^{24}$ −75·6° ⟶ −20·0° (*c*, 0·8 in methanol). Weygand (*loc. cit.*) gives m. p. 124—125°, $[\alpha]_D$ −41·5° (*c*, 0·8 in pyridine).

N-p-*Tolyl*-D-*glucosylamine*.—Owing to its low solubility in anhydrous ethanol D-glucose (10 g., 1 mol.) was suspended in anhydrous methanol (150 ml.). To this was added *p*-toluidine (6 g., 1 mol.) and the mixture was refluxed for 3 hours with the exclusion of moisture. The flask was stoppered and cooled, but as no crystals appeared the methanol was removed under reduced pressure at 35° (moisture excluded). This left a pale yellow syrup which during 5 days deposited N-p-*tolyl*-D-*glucosylamine*, m. p. 135—136°, $[\alpha]_D^{18}$ +208·9° ⟶ −44·6° (after 67 hours) (*c*, 0·7 in methanol) (Found: C, 56·8; H, 6·8; N, 4·9. $C_{13}H_{19}O_5N$ requires C, 58·0; H, 7·1; N, 5·2%). Recrystallisation was attempted, every care being taken that moisture was excluded, but normal *N*-*p*-tolylglucosylamine, m. p. 113°, $[\alpha]_D^{18}$ −97·5° ⟶ −42·7° (*c*, 1·0 in methanol), was obtained.

N-*Phenyl*-D-*glucosylamine*.—On repetition of the above reaction with aniline (1·8 ml., 1·6 mols.) and D-glucose (3 g., 1 mol.), the product obtained had m. p. 134—135°, $[\alpha]_D^{17}$ +53° ⟶ −20·6° (*c*, 0·7 in methanol). *N*-Phenyl-D-glucosylamine, as usually isolated, has m. p. 146° (variable), $[\alpha]_D^{18}$ +10° ⟶ −52° (in methanol).

N-*Phenyl*-D-*galactosylamine*.—(i) Butler, Smith, and Stacey's method of preparing this compound (*J.*, 1949, 3371) was slightly modified as follows. A solution of D-galactose (2 g., 1 mol.) in 0·001N-sulphuric acid (6 ml.) was added to aniline (2 ml., 2 mols.) in ethanol (2·5 ml.), and the mixture left for one day at room temperature. Crystals (1·6 g., 57%) were obtained of *N*-phenylgalactosylamine, m. p. 157—158°, $[\alpha]_D^{18}$ −92° ⟶ −43·5° (*c*, 0·5 in methanol). Butler *et al.* (*loc. cit.*) give m. p. 157—159°, $[\alpha]_D$ −92° ⟶ −37° (*c*, 1·2 in methanol).

(ii) The reaction of galactose and aniline under anhydrous conditions in methanol was attempted as in the case of glucose. The product, which isomerized on recrystallization, was *N*-phenylgalactosylamine, m. p. 141—143°, $[\alpha]_D^{19}$ −22·1° ⟶ −40·3° (*c*, 0·4 in methanol).

N-p-*Tolyl*-D-*galactosylamine*.—The compound, $[\alpha]_D^{18}$ −33·0° ⟶ −14·1° (*c*, 0·2 in methanol), prepared under anhydrous conditions, also differs from the compound prepared in aqueous solution (see below).

N-*Phenyl*-D-*mannosylamine*.—A solution of D-mannose (3 g., 1 mol.) in 0·001N-sulphuric acid (10 ml.) was added to a solution of aniline (3 ml., 2 mols.) in ethanol (4 ml.). After a few hours at room temperature crystals appeared. After 3 hours in the refrigerator *N*-phenyl-D-mannosylamine (4·0 g., 95%), m. p. 181°, $[\alpha]_D^{18}$ −179·3° (*c*, 0·3 in pyridine), $[\alpha]_D^{17}$ −101·4° ⟶ −45·0° (in 70 hours) (*c*, 0·2 in methanol), was collected. Weygand (*loc. cit.*) prepared this compound, m. p. 180—181°, by heating an aqueous suspension of the components.

Ultra-violet Absorption Spectra.—The spectra of *N*-phenylmannosylamine and of *N*-*p*-tolylribosylamines *A* and *B* were measured in methanol over the range 2200—3100 Å. Measurements were made at intervals of *ca.* 24 hours during the time for which mutarotation was proceeding, but no appreciable change in the spectrum was observed. The changes in rotation taking place simultaneously (in methanol) with the absorption measurements were: *N*-phenyl-

mannosylamine, $[\alpha]_D^{17}$ −101·4° ⟶ −45·0° (in 70 hours) (*c*, 0·2 in methanol); *N-p*-tolylribosylamine, *A*, $[\alpha]_D^{21}$ +135·1° ⟶ +12·0° (in 60 hours) (*c*, 0·3 in methanol); *N-p*-tolylribosylamine *B*, $[\alpha]_D^{20}$ +21·8° ⟶ +11·7° (in 62 hours) (*c*, 0·3 in methanol). Spectral data are tabulated.

Compound	Interval after dissolution	$\lambda_{max.}$ (Å)	log $\epsilon_{max.}$	$\lambda_{min.}$ (Å)	log $\epsilon_{min.}$
N-p-Tolylribosylamine *A*	nil	2450	4·47	2680	3·44
		2900	3·72		
	1 day	2450	4·47	2680	3·40
		2900	3·65		
	2 days	2450	4·46	2680	3·37
		2900	3·78		
N-p-Tolylribosylamine *B*	Nil	2500	5·62	2740	3·97
		2950	4·25		
N-Phenylmannosylamine	Nil	2400	4·48	2620	2·68
		2850	3·52		
	1 day	2400	4·49	2620	2·76
		2850	3·53		
	2 days	2400	4·50	2620	2·74
		2850	3·50		

General Preparation of N-p-*Tolylglycosylamines.*—To a solution of the sugar (1 g., 1 mol.) in 0·001N-sulphuric acid (2 ml.) was added a solution of *p*-toluidine (1 g., 1·3 mols.) in absolute ethanol (2·4 ml.). The mixture was left at room temperature until crystallisation appeared to be complete and then placed in the refrigerator for 2 hours. The crystals were collected and purified. The product did not need to be recrystallised. Fructose and sorbose did not react under these conditions, whereas L-arabinose gave a very dark solution from which no crystalline product separated even after evaporation of some of the solvent. The physical constants of the products obtained are tabulated below, together with those recorded for the compounds prepared by other workers using different methods.

N-p-Tolylglycosylamine prepared from:	Approx. time of reaction (days)	Yield (%)	M. p.	Rotation	Previous data: M. p.	Previous data: Rotation	Previous data: Workers (*locc. cit.*)
Ribose	¼	90					
Galactose	2	67	161—162°	$[\alpha]_D^{19}$ −80° ⟶ +8·8° (*c*, 0·2 in methanol)	154—155°	$[\alpha]_D$ −49·5° ⟶ +10·5° (in 83% methanol)	Weygand
Glucose	3	50	107—109	$[\alpha]_D^{16}$ −95·5 ⟶ −42·5 (*c*, 0·4 in methanol)	117—118	$[\alpha]_D^{24}$ −101·2 ⟶ −45·8 (*c*, 0·2 in methanol)	Honeyman and Tatchell
Mannose.....	½	93	183	$[\alpha]_D^{17}$ −101·4 ⟶ −45·0 (*c*, 0·2 in methanol)	183—184	—	Weygand
Xylose	4	38	124—125	$[\alpha]_D^{19}$ −59·0 (*c*, 0·3 in pyridine) $[\alpha]_D^{24}$ −72·2 ⟶ −20·4 (*c*, 0·6 in methanol)	124—125	$[\alpha]_D^{20}$ −41·5 (in pyridine)	Weygand

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273. *Inorganic Chromatography on Cellulose. Part XI.* A Study on the Separation of Tantalum from Niobium and its Application to Quantitative Analysis.*

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A new method is described for the separation of tantalum and niobium from each other and from certain other metals. The method is based on their extraction in turn as fluorides, by ethyl methyl ketone in the presence of cellulose adsorbent. Tantalum is extracted first with ethyl methyl ketone saturated with water. Niobium is then extracted with the same organic solvent containing 7·5% (v/v) of hydrofluoric acid (40% aqueous solution). It has been shown that, so long as the amount of tantalum present does not exceed that of the niobium, a sharp and quantitative separation is obtained. The method has been applied to the separation of the earth acids from their mixtures with other metal ions, and to the determination of niobium and tantalum in minerals and alloys.

The separation of tantalum and niobium together, from other metals is not readily accomplished, particularly from minerals and ores, by existing chemical methods. The quantitative separation of tantalum from niobium may be even more difficult, the method probably most widely employed in analytical chemistry being based on the use of tannin and described in detail by Schoeller ("The Analytical Chemistry of Tantalum and Niobium"). The methods using tannin, however, are difficult and slow in operation and do not always give satisfactory results. Accordingly, attention was directed to chromatographic procedures which have been found valuable in analysis (Arden, Burstall, and Linstead, *J.*, 1949, S 311; Burstall and Wells, *Analyst*, 1951, **76**, 396; Burstall, Davies, Linstead, and Wells, *J.*, 1951, 516; Burstall, Davies, and Wells, *Discuss. Faraday Soc.*, 1949, No. 7, p. 179; Kember and Wells, *Analyst*, 1951, **76**, 570).

Experiments were first made upon complex tantalum and niobium salts with organic acids such as tartrate, citrate, oxalate, and acetate, but these did not prove very satisfactory. With fluorides the method has been found very promising. The method of extraction therefore consisted in getting the niobium and tantalum in solution in aqueous hydrofluoric acid, soaking up this solution in cellulose pulp, and placing the product so formed at the top of a column of cellulose and extracting it with ethyl methyl ketone containing water or aqueous hydrofluoric acid. In this work, platinum vessels were used for preparation of the samples, and Polythene for the chromatographic tube and vessels for collection of fractions. The choice of solvent was determined by tests using a paper-strip technique (Burstall, Davies, Linstead, and Wells, *loc. cit.*); tests were then made with columns packed with cellulose pulp.

It was soon found that the use of ethyl methyl ketone containing a low concentration of hydrofluoric acid favoured the extraction of tantalum, whereas a high acidity was necessary for extraction of niobium; moreover, the presence of ammonium fluoride in the sample "wad" was shown to be beneficial in assisting in the retention of certain other ions present as impurities. Tantalum and niobium were extracted free from impurities which included, calcium, magnesium, thorium, cerium, rare earths, aluminium, iron, and lead, when these were present. In the case of tantalum, no impurity has yet been found which markedly contaminates the extracted fluoride. Other ions which were examined included, tin, zirconium, titanium, tungsten, and manganese. Except for manganese, these ions were found, however, to contaminate appreciably the niobium fraction and work is in progress to reduce this effect. These ions are often present in minerals and ores containing tantalum and niobium.

Quantitative extraction of tantalum and niobium in fluoride solution was difficult. Although it was possible to extract pure tantalum and niobium from a mixture of the two metals by using ethyl methyl ketone containing up to 2% and 7·5% of hydrofluoric acid respectively, neither element could be quantitatively extracted with these solvents, even

* Part X, *Analyst*, in the press. The work described in Part XI was presented in part at the XIIth International Congress of Pure and Applied Chemistry, New York, September, 1951.

when each was present alone. A systematic study was therefore begun in order to find whether solvents based on the use of ethyl methyl ketone, water, and hydrofluoric acid, could be found which would completely extract the fluorides. With tantalum, the best separation was obtained with ethyl methyl ketone saturated with water and a sample solution containing 25% v/v of hydrofluoric acid (40% w/w solution). In the absence of niobium the recovery of tantalum was of the order of 97%, but in the presence of niobium in amounts equal to or in excess of the tantalum it was quantitative. Addition of hydrofluoric acid to the solvent decreased the recovery of tantalum, and increase in the volume of solvent employed did not improve it. As the amount of hydrofluoric acid in the solvent was increased, the recovery of tantalum decreased still further and with solvent acidity of 20% hydrofluoric acid, the recovery was less than 30%. It thus appeared that the best conditions for the extraction of tantalum necessitated the presence of the minimum quantity of hydrofluoric acid in the chromatographic system. In the presence of niobium a considerable volume of solvent could be employed in excess of that required for extraction of tantalum without causing extraction of niobium, thus ensuring ideal conditions for sharp separation of the two elements.

Experiments on the extraction of niobium indicated that a high concentration of hydrofluoric acid in the solvent was necessary and that the movement of niobium increased with increasing acid concentration. The most convenient concentration of hydrofluoric acid so far found was 7·5% (v/v, 40% aqueous solution). In the presence of niobium only, it was impossible to effect quantitative extraction directly by employing the solvent containing hydrofluoric acid solution: it was necessary to wash the column first with the ethyl methyl ketone–water solvent in the manner employed for extraction of tantalum. Under these conditions extraction of niobium was quantitative.

On employing mixtures of tantalum and niobium in amounts up to 150 mg. of each, provided that the tantalum did not exceed niobium, separations were quantitative and the earth acids were of high purity. When tantalum is present in excess of niobium there is a small retention of tantalum in the column. A similar retention may be obtained (of the order of 4—5%) when tantalum is present with other metal ions. Spectrographic analyses have shown that extraction of other metal ions (so far examined) with the tantalum is very small. The main difficulty with niobium is the prevention of partial extraction of titanium and zirconium and, to a less extent, tin and tungsten, when these elements are present.

The chromatographic technique has been examined so far for the determination of tantalum and niobium in mixtures with one another and when present together with calcium, magnesium, lead, aluminium, iron, manganese, lanthanons (including cerium), and thorium. Recent work has shown that movements of titanium, zirconium, and tin can be greatly suppressed by the use of a low acidity solvent (2% HF) after removal of tantalum but before extraction of niobium with solvent containing 7·5% of hydrofluoric acid. Research on this aspect is continuing.

The method has been applied to the analysis of columbite, pyrochlore, and ferro–tantalum–niobium alloys.

The mechanism underlying the extraction and separation of tantalum and niobium from each other and from other metals has not been fully elucidated. It is a prerequisite for this chromatographic method, however, that the fluorides of tantalum and niobium should be soluble in the respective solvents used for extraction, but since niobium is removed in succession to tantalum, it is essential that niobium be retained during extraction of tantalum. It is reasonable to suppose that the fluorides of these metals are present as complex salts or acids of the type $R(TaF_6)$ or $R_2(TaF_7)$ and $R_2(NbF_7)$ or $R_2(NbOF_5)$ which are the commonest and most stable complexes formed in solution. Under these conditions of extraction for tantalum, it is supposed that complex tantalum fluoride, probably in association with water and solvent molecules, is extracted as one of the foregoing types of salt, whereas niobium is in the form of the oxyfluoride. However, with solvent containing hydrofluoric acid used for niobium extraction, it is possible for conversion of a niobium oxyfluoride into a salt of the type $R_2(NbF_7)$ to take place; this is then extracted. It is well established that water and hydrofluoric acid content of the solvents

are critical factors. Partition between complex fluoride in the organic solvent and water in the cellulose adsorbent is probably an important factor in the separation process. Chemical adsorption between complex fluorides and reactive groups in the cellulose may also play a part and may be responsible for the small retention of tantalum observed in the extraction process.

Experimental

I. *Paper-strip Experiments.*—A number of paper-strip extractions were carried out by a standard technique which has been widely employed for separation of many inorganic ions. Polythene boats were, however, employed as solvent containers to prevent silica contamination by the action of hydrofluoric acid on glass vessels. Several different solvents were employed in order to obtain an indication of the feasibility of the separation under consideration and to compare the relative values of the various solvents. It was decided to limit the preliminary investigations to the separation of tantalum and niobium from one metallic impurity. The impurities which were expected to cause difficulty were zirconium, aluminium, iron, titanium, and tin. Titanium was selected from this list for these experiments as the metal most likely to be troublesome.

The procedure adopted was to run two strips simultaneously, one with a fluoride solution of titanium and the other with a fluoride solution of tantalum and niobium. The strips were developed by spraying with tannin solution, followed by exposure to ammonia vapour. A comparison was then made of the distances moved by the titanium on the one hand and the tantalum and niobium on the other.

The solvents examined included a number of esters, ethers, alcohols and ketones, all with the addition of 5% (v/v) of hydrofluoric acid (40% aqueous solution). Of these, the alcohols and ketones caused considerable movement, the ethers a small amount, and the esters practically none. Of the solvents tried, ethyl methyl ketone gave the best separation and was therefore employed for further experiments. A number of strips were then run using a mixture of all three of the metals, tantalum, niobium, and titanium, and the effect of addition of measured quantities of 40% of hydrofluoric acid to the solvent was examined. Strips were run with concentrations of 2, 5, and 10% (v/v) of this acid in the solvent. In all cases, separation into bands was obtained, but the movement of titanium appeared to increase with increasing hydrofluoric acid concentration and the bands became less sharply defined.

II. *Cellulose-column Experiments.*—(1) *Ethyl methyl ketone employed for extractions.* The ethyl methyl ketone used throughout this work was the purified commercial product. Five gallons were digested under reflux with a mixture of 60 g. of potassium permanganate and 100 g. of sodium hydrogen carbonate in 3 l. of water for about 2 hours. The aqueous layer was removed and the solvent layer dried first over calcium chloride and then over sodium hydroxide. The ethyl methyl ketone was then distilled.

(2) *Preparation of sample solution.* In these experiments, pure tantalum and niobium metals or oxides were employed and any other metals added as impurities were usually taken as oxides. Solution was effected by dissolving the metal or oxides in about 10 ml. of hydrofluoric acid (40% w/w) solution with a few drops of concentrated nitric acid in addition. By covering the dish with a platinum cover and gently warming it before repeated evaporations with hydrofluoric acid, solution of the tantalum and niobium was easily effected. The solution was finally evaporated just to dryness after removal of nitric acid by evaporation with hydrofluoric acid and was then taken up in the requisite volume of dilute hydrofluoric acid solution (usually 6 ml. of water and 2 ml. of 40% acid solution). A clear solution was not, of course, obtained with samples containing metal ions added as impurities and which formed insoluble fluorides.

(3) *Extraction technique.* A tube was constructed from Polythene to a pattern similar to that of the glass columns used for the extraction of uranium (*Analyst*, 1951, **76**, 396), and the cellulose pulp used was the standard grade as supplied by Messrs. Reeve Angel Ltd. Full details of the procedure for extraction are given on p. 1501.

(4) *Preliminary experiments.* Early experiments showed that tantalum and niobium could be extracted by ethyl methyl ketone containing hydrofluoric acid (40% w/w aqueous solution), in concentration ranging from 0 to 7·5% v/v, but it was found that titanium was also extracted. The movement of titanium was examined because it forms a water-soluble fluoride and is commonly associated with the earth acids in naturally occurring materials.

The effect of the addition of complexing agents to the sample was investigated before attempting to find conditions for complete extraction of tantalum and niobium but with retention of titanium. After examination of a number of fluorides, it was found that ammonium fluoride

largely prevented the movement of titanium but permitted extraction of the earth acids; moreover, there were indications that tantalum could be separated from niobium by altering the acidity of the organic solvent. A series of experiments was therefore made in which conditions were sought for complete extraction of tantalum and niobium from a number of commonly associated ions. It was hoped then to find conditions for what was at the time considered to be possibly the more difficult separation, namely, that of the tantalum from the niobium.

A synthetic mixture was prepared consisting of equal amounts of an aluminium-iron silicate (granitic material), thoria, lanthanons isolated from monazite, alumina, ferric oxide, tin oxide, titanium oxide, and zirconium oxide. To 1-g. amounts of this mixture, known amounts of tantalum and niobium were added as metals (usually about 150 mg.) and the whole was decomposed as described in (2) (above). After final evaporation to dryness, 8 ml. of a solution of hydrofluoric acid (40%), in concentrations varying from 25 to 100% in different experiments, were added together with 1 g. of ammonium fluoride. Extractions were made in cellulose columns with ethyl methyl ketone containing 7·5% v/v of hydrofluoric acid (40%). Although tantalum and niobium were both extracted with a very good degree of purity with respect to other ions, in no case could quantitative recovery be obtained. Moreover, results were erratic and recoveries were generally poor. There appeared to be continuous extraction of the earth acids up to a volume of 600 ml. of solvent but increase in this volume brought about little further extraction. The process for extraction in the absence of foreign ions was then examined but results again were generally disappointing. Similar erratic results were obtained when tantalum and niobium were taken separately. There appeared to be no relation between the acidity of the sample solution and the amount of acid in the solvent. A systematic investigation of the conditions required for extraction of tantalum when present alone or with ions other than niobium was then carried out and this was followed by an investigation of the extraction of tantalum and niobium from their mixtures with one another.

(5) *Extraction of tantalum.* The first experiments were carried out in order to find the effect of the hydrofluoric acid concentration in the solvent on the degree of extraction of tantalum. These showed that, as the acidity of the solvent decreased, better recoveries of tantalum were obtained. It was also found that the presence of water in the solvent was advantageous and that a low-acidity sample was better. It was found that the minimum acidity and volume conditions for the sample solution which could be reasonably employed consisted of 2 ml. of aqueous hydrofluoric acid solution (40%) and 6 ml. of water (with 1 g. of ammonium fluoride added). Recoveries from 150 mg. of tantalum ranged from 93% down to about 30% when the acidity of the solvent was varied from 1% up to 10% of hydrofluoric acid (v/v) and at the high acidities results tended to be erratic. Results were similar in the presence and absence of foreign ions. Usually no further extraction of tantalum occurred after a volume of 200—300 ml. of solvent had been passed. Extraction with solvent containing water in addition to the acid usually resulted in a better extraction of tantalum.

TABLE 1.

Ta added, g.	Nb added, g.	Base material present *	Ta found, g.	Analysis of Ta
0·155	nil	nil	0·149	—
0·151	0·149	nil	0·149	<0·1% Nb
0·148	0·154	nil	0·147	"
0·156	0·005	nil	0·143	—
0·153	0·047	nil	0·140	—
0·149	nil	1 g., No. 3	0·148	—
0·152	0·151	1 g., No. 3	0·148	<0·1% Nb 0·03% Fe
0·151	nil	1 g., No. 2	0·147	0·1% Fe, <0·1% Ti
0·153	nil	1·4 g., No. 4	0·150	0·02% Fe
0·133	nil	1 g., No. 1	0·131	0·03% Fe, 0·01% Ti
0·150	0·153	1 g., No. 1	0·147	0·01% Sn, <0·1% Zr

* *No.* 1 : equal amounts of aluminium silicate, ThO_2, TiO_2, SnO_2, ZrO_2, Fe_2O_3, lanthanons, cerium (from monazite), Al_2O_3. *No.* 2 : equal amounts of Al_2O_3, Fe_2O_3, ThO_2, lanthanons, cerium, TiO_2. *No.* 3 : equal amounts of Al_2O_3, Fe_2O_3, ThO_2, lanthanons, cerium. *No.* 4 : equal amounts of Al_2O_3, Fe_2O_3, ThO_2, lanthanons, cerium, CaF_2, MnO_2, PbO, MgO.

In view of these results it was decided to examine the degree of extraction with ethyl methyl ketone saturated with water but containing no added hydrofluoric acid. This solvent contains approximately 10% of water (by vol.), the exact value depending upon the temperature of the experiment. It was soon found that better extractions of tantalum were obtained than were hitherto possible, and therefore the conditions of employing this solvent were more critically

examined. The results given in Table 1 are typical of many showing the degree of extraction from samples containing tantalum alone, or in the presence of other ions, or present with niobium.

The sample was prepared in a volume of 8 ml. of 25% v/v hydrofluoric acid (40%) with 1 g. of ammonium fluoride added, and it was then absorbed in 6 g. of standard-grade cellulose (Reeve Angel Ltd.) and extracted on a column of cellulose (12″ long). Ethyl methyl ketone saturated with water (300 ml.) was employed for extraction although it was usually found that no further extraction of tantalum was obtained after taking 250 ml. Spectrographic results of the analysis of the recovered tantalum are also given in Table 1.

The results show that when tantalum is present alone or together with relatively small amounts of niobium, recoveries are of the order 92—96%, indicating appreciable hold-up of tantalum. However, when tantalum is present with equivalent amounts of niobium or with other foreign ions, the recoveries are reasonably good, being of the order of 98—99%. In all cases spectrographic analyses showed that the extracted tantalum was of a high degree of purity.

(6) *Extraction of niobium.* Preliminary experiments showed that niobium could only be extracted as fluoride in a reasonable volume of solvent by employing high concentrations of hydrofluoric acid in the ethyl methyl ketone solvent, but later work with solvent containing 7·5% of hydrofluoric acid (40%) and employed directly for extraction gave erratic results. It was found, however, that when this solvent mixture was employed after treatment of the column with the solvent used for tantalum extraction, excellent recoveries of niobium were obtained. The reason for this interesting effect has not yet been elucidated but in later experiments the solvent used for tantalum extraction was always employed before that used for extraction of niobium, with beneficial results.

(7) *Quantitative separation of tantalum from niobium.* It has been shown (see Table 1) that complete extraction of tantalum when present alone could not be achieved under the conditions which have been described, but, in the presence of niobium in amount at least equal to that of the tantalum, very good recoveries were obtained. A series of experiments was therefore carried out in which separations were made of tantalum and niobium mixtures (niobium present in similar or greater amount). Tantalum was extracted by using 300 ml. of ethyl methyl ketone solvent (saturated with water) and niobium was then extracted with 400 ml. of ethyl methyl ketone containing 7·5% (v/v) of hydrofluoric acid (40%). No advantage was gained by increasing the volume of 400 ml. of solvent for niobium.

(8) *Method for the determination of tantalum and niobium in their mixtures.* Ethyl methyl ketone was purified as described on p. 1499.

Preparation of Solvent A (as employed for extraction of tantalum). A solution of ethyl methyl ketone saturated with water was prepared by shaking intermittently for about 30 minutes 400 ml. of the solvent with 50 ml. of water in a separating-funnel. When excess of water had completely separated and the organic solvent was clear, the aqueous layer was run off and discarded.

Preparation of Solvent B (as employed for extraction of niobium). A volume of 7·5 ml. of hydrofluoric acid solution (40%) was added to each 92·5 ml. of ethyl methyl ketone, a Polythene measuring cylinder being used. A Polythene bottle was employed for storage of the prepared solvent.

Procedure: Chromatographic extractions. Tantalum and niobium metals or oxides were accurately weighed into a platinum dish and moistened with water, and a few drops of nitric acid followed by 5—10 ml. of hydrofluoric acid (40%) solution were added; decomposition was then continued as described in (2) (p. 1499), and the dry residue was taken up as before but with addition of 1 g. of ammonium fluoride. The mixture was covered and gently warmed for ten minutes to ensure solution of tantalum and niobium fluorides, care being taken to avoid appreciable evaporation. A Polythene rod was used for stirring the contents of the dish. A column of activated cellulose (standard grade, Reeve Angel Ltd.) about 12 in. long was prepared in a Polythene tube (*ca.* 2 cm. bore, 26 in. long) at the top of which was a funnel to facilitate introduction of the sample. The bottom of the tube terminated in a short length of narrow tubing of about 50-mm. bore which was sealed by a 6-cm. length of polyvinyl chloride tubing with a screw slip. The column was prepared by adding a slurry of the cellulose in ethyl methyl ketone. The cellulose settled under its own weight and the level of the solvent was allowed to fall to the top of the column. A homogeneous column was thus obtained. The column was conditioned by passage of 100 ml. of Solvent A which was finally allowed to fall to the level of the cellulose. Cellulose (6 g.) was added to the sample solution in its platinum dish and the whole well mixed, a Polythene rod being used in order to form a homogeneous friable mass. The mixture was then introduced into the top of the column, and the empty platinum dish allowed to rest in the funnel throughout the subsequent procedure. Solvent A was added in

sufficient amount to reach a level about 2 cm. above the cellulose containing the sample. The wad was then agitated by means of a Polythene plunger so that it formed a homogeneous continuation of the main column. The plunger was washed with Solvent A, sufficient being used to reach nearly to the top of the tube (to funnel-join). When this first batch of Solvent A had reached the level of the cellulose the addition of solvent was continued until a quantity of 300 ml. had been passed. The eluent, containing the tantalum fraction, was collected in a 600-ml. Polythene beaker. When the last of Solvent A had fallen to the level of the cellulose, the beaker was replaced by another similar beaker. Sufficient of Solvent B was poured first into the dish and then into the column in order to come about halfway to the level of the top of the column. It was then allowed to fall to the level of the cellulose. A further similar quantity of solvent was added and the sample was gently beaten with the plunger, care being taken not to penetrate below the actual sample "wad." The plunger was washed with Solvent B, and the extraction of niobium continued as for tantalum, but 400 ml. of solvent were collected.

Removal of solvents and determination of tantalum and niobium. The solvent was removed from each fraction, in a fume cupboard by cautious evaporation under an infra-red lamp, a stream of air being directed into the beaker during evaporation. When the volume of solution had been sufficiently reduced, the contents of the beaker were transferred to a platinum dish and evaporated further to remove the remaining solvent, care being taken to avoid spray. Sulphuric acid (5 ml. of 1 : 1) was then added, followed by 2 ml. of concentrated nitric acid and about 1 ml. of 70% perchloric acid. The solution was evaporated gently to sulphuric acid fumes. The contents of the dish were washed into a 250-ml. glass beaker, the volume at this stage being about 50 ml. After addition of 5 g. of ammonium chloride, the solution was heated to boiling; 0·5—2 g. of tannin (depending on the amount of earth acid present), dissolved in about 5 ml. of hot water, was then added and sufficient solid ammonium acetate to give a solution of pH 4—5 (by test-paper). The beaker was kept at about 80° for about 10 minutes, and the precipitate collected on a No. 541 Whatman filter-paper. The precipitate was finally strongly ignited to oxide, at a temperature preferably above 1000° (Ta_2O_5 or Nb_2O_5). The oxides were spectrographically analysed for impurities. In the recent stages of the work it has been found that this more lengthy tannin procedure could be replaced by a shorter procedure involving direct ignition to the oxides. After removal of solvent and evaporation to a few ml. in a platinum dish, a few drops of 50% sulphuric acid and concentrated nitric acid were added, evaporation continued to about 1 ml., and sufficient ashless cellulose "block" added to absorb the solution. The whole was then carefully ignited to the oxide. This shorter procedure was not employed when the amount of tantalum or niobium present was less than about 5 mg.

TABLE 2.

Expt. no.	Ta, mg.: Taken	Ta, mg.: Found	Nb content of Ta, mg.	Nb, mg.: Taken	Nb, mg.: Found	Ta content of Nb, mg.
1	151·0	149·0	0·15	151·0	—	—
2	50·5	52·0	0·05	150·0	150·5	0·3
3	10·3	10·4	0·01	152·1	153·0	0·15
4	5·0	6·2	0·03	153·1	152·9	0·15
5	nil	0·7	—	152·2	154·4	0·15
6	150·9	151·6	0·15	150·2	151·4	0·15
7	2·0	1·9	0·002	11·1	11·4	—
8	147·9	146·7	0·30	154·2	150·2	0·15
9	49·5	48·7	0·15	154·6	155·5	0·50
10	6·1	6·1	0·03	157·1	157·5	0·15
11	152·4	149·3	0·20	251·5	253·4	1·80

Table 2 shows the results obtained on a range of mixtures. Spectrographic analyses were carried out to determine the niobium and tantalum contents, respectively, of the separated tantalum and niobium oxides. The results indicate that tantalum and niobium can be quantitatively separated from each other in good purity (provided that the amount of tantalum present in the original mixture does not exceed that of the niobium). For high Ta : Nb ratios the procedure is still under investigation, but even in the absence of niobium, tantalum extraction exceeds 90%. It will be seen later, however, that application of the procedure to complex mixtures with other ions leads to a better recovery of tantalum than in the absence of niobium.

(9) *The separation and determination of tantalum and niobium in their mixtures with other ions.* It was established early in the work on the study of the movements of other ions in association with tantalum and niobium that ammonium fluoride would prevent the movement of soluble fluorides such as those of titanium, tin, and zirconium under certain conditions. These conditions were obtained when a direct extraction was made with ethyl methyl ketone containing hydro-

fluoric acid (40%) without addition of water. Unfortunately, there was only partial extraction of niobium. Good and consistent recoveries of niobium were only obtained when the solvent used for tantalum extraction was passed through the column before the extraction with solvent used for niobium as in the procedure already described. It was shown, however, that, of the many ions examined, only traces were extracted with the tantalum, whereas extraction of niobium caused the extraction of certain impurities, mainly titanium, tin, and zirconium, in sufficient amount appreciably to contaminate the niobium fraction. Extraction of commonly occurring ions such as Ca, Mg, Pb, Mn, Th, Fe, Al, Ce, and rare earths was very small. The degree of extraction of titanium, tin, and zirconium was also affected by the amount of the niobium. Experiments have shown that the degrees to which these ions may cause contamination are in the order Ti, Zr, and Sn (least). The work which follows consists of a preliminary survey of the applications of the chromatographic technique to the analysis of complex mixtures of tantalum and niobium. In all cases the initial sample was decomposed by treatment with nitric and hydrofluoric acids with final conversion into fluorides in the manner described on p. 1499. Where insoluble fluorides were present, these were dispersed into the cellulose wad in the same manner as the solution.

A mixture of equal amounts of iron, aluminium, thorium, lanthanons (including cerium), and aluminium silicate was prepared by taking equal amounts of the corresponding oxide (except in the case of aluminium silicate which was added as a naturally occurring silicate). Results obtained for recoveries of added tantalum and niobium from 1 g. of the mixture are given in Table 3. Spectrographic analyses of the separated tantalum and niobium oxides are also shown.

TABLE 3.

Ta, mg. : Added	Found	Impurities in Ta recovered, mg.	Nb, mg. : Added	Found	Impurities in Nb recovered, mg.
149·3	147·7	0·1 Fe	nil	—	—
nil	—	—	151·5	150·4	0·4 Fe
151·7	148·6	0·15 Nb	150·9	150·6	0·4 Ta 0·15 Fe
5·6	5·0	0·1 Nb 0·3 Fe	30·0	31·5	0·1 Ta 0·4 Fe
20·2	19·5	0·1 Nb 0·2 Fe	100·5	100·9	0·2 Ta 0·3 Fe

TABLE 4.

Ta (or Ta fraction), mg. : Added	Found	Impurities in Ta (or Ta fraction), mg.	Nb (or Nb fraction), mg. : Added	Found	Impurities in Nb (or Nb fraction), mg.*
(*a*) 1 G. of mixture used in Table 3 plus 125 mg. of TiO_2.					
150·6	147·5	0·2 Ti 0·2 Fe	nil	40 as oxide	Ta = 2 Fe = 1·5 Ti = 30
(*b*) 1 G. of mixture used in Table 3 plus 125 mg. of ZrO_2.					
149·8	144·8	0·2 Zr 0·2 Fe	nil	27 as oxide	Ta = 2·5 Fe = 0·8 Zr = 20
nil	nil	—	149·4	162	Fe = 0·6 Zr = 12
(*c*) 1 G. of mixture used in Table 3 plus 125 mg. of SnO_2.					
150·1	144	Sn, nil	nil	21 as oxide	Ta = 1 Fe = 1·2 Sn = 15
nil	nil	—	150·0	161	Fe = 5 Sn = 5
(*d*) 1 G. of mixture used in Table 3 plus 0·1 g. of each of Ca, Mn, Pb, Mg as oxides.					
153·1	150·1	all impurities 0·3 mg.	nil	7 as oxide	—
nil	3	—	155·0	154	Fe = 0·3 Mn = 1·5

* Approximate spectrographic analysis.

It was found necessary to increase to 500 ml. the volume of solvent employed for extraction of niobium in the presence of impurities.

Experiments have also been carred out with mixtures containing titanium, zirconium, and tin in addition to iron, aluminium, thorium, and rare earths. The results are shown in Table 4.

The results given in Tables 3 and 4 show that there is only very slight contamination of

extracted tantalum, the lowest recoveries being obtained from mixtures containing Ti, Zr, or Sn. Part of the remaining tantalum could be recovered from the niobium fraction. Good recoveries of niobium appear to be obtained in all cases but contamination by Ti, Zr, and Sn is appreciable.

Research is in progress to overcome the interference by Ti, Zr, and Sn and also to improve the recovery of tantalum. This work involves a second chromatographic extraction of the niobium fraction under modified solvent conditions. It has been found that complete removal of the aqueous solvent used for tantalum by washing the column with ethyl methyl ketone containing 2% of hydrofluoric acid before extraction with the solvent containing 7·5% of the acid leads to a marked reduction in the movements of Ti, Zr, and Sn. The movements of these metals in the presence of niobium, however, have yet to be examined and also the effect on recovery of niobium. [*Added*, 6.3.52: Difficulties due to interference by Ti, Zr, and Sn have now been overcome. A modified procedure will shortly be submitted for publication.]

(10) *Application of the chromatographic procedure to minerals and alloys.* The process has not yet been widely applied to naturally occurring materials but results have been obtained on samples of pyrochlore, columbite, and synthetic ferro–tantalum–niobium alloy. Results obtained on a sample of each of these materials are given below. Since all samples were fairly complex materials, a second chromatographic separation of the niobium fraction was made in two instances in order to reduce contamination by impurities such as titanium and also to recover small amounts of tantalum which were not extracted with the main tantalum fraction but were all or partly extracted with the niobium.

(a) *Columbite.*—Wt. of sample = 0·5 g. Decomposed by HF and HNO_3 (insoluble, fused with $KHSO_4$—tannates precipitated—ignited and added to soluble portion).

Chromatographic separation. Tantalum fraction = 146·7 mg. of oxides, contained: 0·1 mg. Nb, 0·1 mg. Fe, and 0·7 mg. Zr (as oxides) (*i.e.*, total impurity = 0·9 mg.). Niobium fraction = 192 mg. oxides. (500 Ml. of solvent used.)

The niobium fraction was subjected to a second chromatographic extraction in order to decrease contamination by Ti, Sn, Zr and recover any tantalum which had passed through in the first separation.

Tantalum fraction = 7·6 mg., contained 0·4 mg. of total impurity. Niobium fraction = 183 mg., contained: 0·2 mg. Ta, 0·2 mg. Fe, 0·2 mg. Sn, 1·8 mg. Ti, and 0·4 mg. Zr (as oxides).

Total Ta_2O_5 = 30·9% (0·3% impurities).

Total Nb_2O_5 = 36·6% (0·4% TiO_2 and 0·2% other impurities).

(b) *Pyrochlore Concentrate.*—Wt. of sample = 0·4992 g. Decomposed by HF–HNO_3.

Chromatographic separation. Tantalum fraction = 20·0 mg. of oxides, contained: 0·1 mg. Nb, 0·2 mg. Fe, 0·02 mg. Zr, 0·1 mg. Sn, 0·2 mg. Ti (as oxides) (*i.e.*, total impurity = 0·5 mg.). Niobium fraction = 245·9 mg. oxides, contained: 0·3 mg. Ta, 0·2 mg. Fe, 0·3 mg. Zr, 0·5 mg. Sn, 12 mg. Ti (as oxides).

Total Ta_2O_5, 4·0% (0·1% impurities).

Total Nb_2O_5, 49·2% (2·4% TiO_2, 0·2% other impurities).

This analysis illustrates the degree of contamination of the separated niobium by titanium. A second chromatographic extraction was not carried out but experiments have shown that this would have effected a considerable reduction in titanium.

(c) *Ferro-tantalum–Niobium Alloy.*—Contains mainly Ta–Nb–Fe, Mn.—Wt. of sample = 0·3719 g. Decomposed by HF + HNO_3.

Chromatographic separation. Tantalum fraction = 58·5 mg. of oxides, contained: <0·1 mg. Nb, 0·1 mg. Fe, <0·1 mg. Mn, <0·1 mg. Sn, <0·1 mg. Ti, <0·1 mg. Zr (as oxides) (*i.e.*, total impurity <0·5 mg.). Niobium fraction = 286·5 mg. oxides. (500 Ml. of solvent used.)

As in example (*a*), the Nb fraction was subjected to a second chromatographic extraction to recover any Ta which had passed through in the first separation and reduce contamination of the niobium fraction.

Tantalum fraction = 2·0 mg., contained 0·1—0·2 mg. Fe (as oxide). Niobium fraction = 274 mg., contained <0·2 mg. Ta, 0·2 mg. Fe, approx. 1 mg. Mn, 0·2 mg. Sn, 0·5 mg. Ti, <0·2 mg. Zr and W—detected (as oxides).

Total Ta_2O_5 = 60·5 mg. = 13·33% Ta (<0·2% impurities).

Total Nb_2O_5 = 274 mg. = 51·56% Nb (about 0·5% impurities).

These results suffice to show that the chromatographic technique has considerable promise for the analysis of complex ores and materials containing tantalum and niobium. Further experiments are in progress, particularly on the application of the chromatographic procedure to the analysis of low-grade materials (*i.e.*, less than 1·0% of earth oxides).

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274. *A Synthesis of Flavone Glycosides.*

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Previous methods for the synthesis of flavone glycosides are briefly reviewed. The possibility has been investigated of preparing such compounds from tetra-acetyl glucosyloxy-*o*-aroyloxyacetophenones by molecular rearrangement to the related 1 : 3-diketones and thence by cyclisation and hydrolysis to the glucosyloxyflavone. 7-β-D-Glucosyloxyflavone has been thus prepared, but the method is of very limited scope.

Although the flavones have for long been intensively investigated in many laboratories, very little work is recorded on the preparation of flavone glycosides, and only two essentially different methods have been used.

The first, which consists in the formation of a glycoside of a preformed hydroxyflavone, using, for example, tetra-acetyl α-glucosyl bromide followed by deacetylation, is unsuitable in the general case of di- and poly-hydroxylated flavones. Hattori (*Acta Phytochim.*, 1928, **4**, 63; *A.*, 1928, 1020) used it to prepare 7- and 4′-β-D-glucosyloxyflavones, and Zemplén, Bognár, and Mechner (*Ber.*, 1944, **77**, 99) were able to synthesise 7-β-D-glucosyloxy-5-hydroxyflavone (toringin) from 5 : 7-dihydroxyflavone (chrysin) by taking advantage of the known inhibiting effect of the carbonyl group on alkylation of the hydroxyl group in position 5.

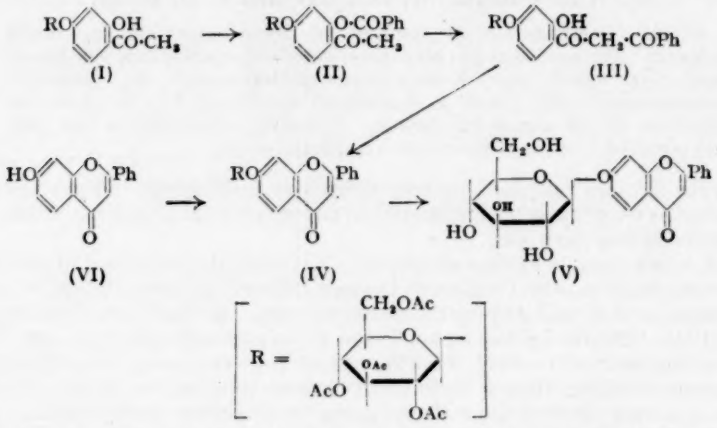
The second method, which is of much wider application but gives very poor yields in the final stage, starts from a fully acetylated flavanone glycoside which is brominated in position 3 and then treated with alkali, to give the flavone glycoside. This method has been used in the preparation of 5 : 3′-dihydroxy-4′-methoxy-7-rutinosyloxyflavone (diosmin) from the related flavanone (hesperidin) (Zemplén and Bognár, *Ber.*, 1943, **76**, 452), and of 5-glucosyloxy-7 : 4′-dihydroxyflavone from the flavanone salipurposide (Zemplén and Mester, *Ber.*, 1943, **76**, 776). A considerable improvement was introduced by Narasimhachari and Seshadri (*Proc. Indian Acad. Sci.*, 1949, **30**, 151) who found that flavanone glycosides, preferably those containing a free phenolic group in position 5, are smoothly oxidised to flavone glycosides by iodine in boiling ethanol in presence of sodium acetate.

Before the publication by Narasimhachari and Seshadri we had begun experiments to see if the Baker–Venkataraman base-catalysed rearrangement of *o*-aroyloxyacetophenones to *o*-hydroxydibenzoylmethanes could be adapted to the synthesis of flavone glycosides (see Baker, *J.*, 1933, 1382; Mahal and Venkataraman, *Current Sci.*, 1933, **2**, 214). An account of this work is now given, but the method is of limited scope and inferior to the potentially versatile synthesis from a flavanone glycoside which may be either natural (cf. Zemplén *et al.*, *loc. cit.*) or synthetical (Reichel and Steudel, *Annalen*, 1942, **553**, 83), followed by oxidation with iodine according to Narasimhachari and Seshadri.

Preliminary experiments with 2 : 4-dibenzoyloxyacetophenone showed that the most suitable basic reagent which might be used in the case of an acetylated glycoside for bringing about molecular rearrangement to a *o*-hydroxydibenzoylmethane [cf. conversion of (II) into (III)] was anhydrous potassium carbonate in pyridine, although the yield of the pure product was only 30% (cf. Doyle, Gógan, Gowan, Keane, and Wheeler, *Proc. Roy. Dublin Soc.*, 1948, **24**, 291, who have discussed the mechanism of this reaction and the different bases which may be used). The next step, cyclodehydration of the 1 : 3-diketone to the flavone [cf. conversion of (III) into (IV)] cannot, in the case of a glycoside, be carried out in the usual way with hydrochloric acid in acetic acid, but it was found that the reaction could be satisfactorily effected by heating the diketone in xylene with a trace of toluene-*p*-sulphonic acid. In this manner 4-benzoyloxy-2-hydroxydibenzoylmethane gave 7-benzoyloxyflavone in good yield.

The preparation of 7-β-D-glucosyloxyflavone (V) was then achieved as follows. 2-Hydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone (I) reacted with benzoyl chloride in pyridine to give the *O*-benzoyl derivative (II), and this underwent rearrangement, when heated with potassium carbonate in pyridine, to the 1 : 3-diketone (III).

Cyclisation in boiling xylene with toluene-*p*-sulphonic acid yielded 7-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)flavone (IV) which was identical with a specimen prepared from



7-hydroxyflavone (VI) and 2 : 3 : 4 : 6-tetra-acetyl α-D-glucosyl bromide. Finally de-acetylation with a trace of sodium methoxide in methanol–chloroform gave, from both specimens of (IV), 7-β-D-glucosyloxyflavone (V). Molecular rearrangement of the benzoyl derivative (II) with potassium hydroxide in pyridine gave an isomeride of the diketone (III); this is probably an enolic form. Similar phenomena were obtained by molecular rearrangement of resacetophenone dibenzoate which, on occasion, gave a 1 : 3-diketone whose initial melting point of 210° fell to 167° on storage (this paper), and by 2-benzoyloxy-4-methoxypropiophenone which reacted with potassium hydroxide in pyridine to give a diketone, m. p. 166° falling to 144° after being kept (Mr. D. Weight, unpublished observation).

Attempts to apply these reactions to the synthesis of 7-β-D-glucosyloxy-5-hydroxy-flavone (toringin) were not successful. Treatment of 2 : 6-dihydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone with two equivalents of benzoyl chloride gave only the monobenzoyl derivative, 2-benzoyloxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)-acetophenone, and treatment of this with potassium carbonate and pyridine led to the isolation of only the debenzoylated product (note that the Baker–Venkataraman transformation had not been effected with a compound containing a free phenolic group).

Experimental

4-Benzoyloxy-2-hydroxydibenzoylmethane.—Resacetophenone dibenzoate (5 g.), anhydrous potassium carbonate (4 g.), and dry pyridine (10 c.c.) were heated on the steam-bath for 1 hour, cooled, poured into water, and acidified to pH 6 with glacial acetic acid. The solid benzoyl-(4-benzoyloxy-2-hydroxybenzoyl)methane crystallised from benzene–methanol as yellow needles (1·37 g., 27%), m. p. 165—167° (Baker, *loc. cit.*, gives m. p. 167°). In some preparations the material, when first isolated, had m. p. *ca.* 210°, but after some time the m. p. had dropped to 167°; this phenomenon is probably due to prototropic change.

7-Benzoyloxyflavone.—4-Benzoyloxy-2-hydroxydibenzoylmethane (1·5 g.) was boiled under reflux in a Soxhlet apparatus in xylene (50 c.c.) containing a trace of toluene-*p*-sulphonic acid; the cup contained anhydrous magnesium sulphate. After 10 hours the xylene was removed under diminished pressure and the residue was crystallised from ethanol, giving 7-benzoyloxyflavone (1·12 g., 79%), m. p. 155—157° (Baker, *loc. cit.*, gives m. p. 157—158°).

2-Benzoyloxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone (II).—Benzoyl chloride (5 c.c.) was added to a solution of 2-hydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)-acetophenone (I) (20 g.; Reichel and Steudel, *loc. cit.*) in anhydrous pyridine, and after 24 hours the solid was collected, dried, and crystallised from ethanol, giving *2-benzoyloxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone* (16 g., 66%) as platelets, m. p. 186—187°, $[\alpha]_D^{17}$ −18·6° (*c*, 2·5 in acetone) (Found: C, 59·4; H, 5·3. $C_{29}H_{30}O_{13}$ requires C, 59·4; H, 5·2%).

2-Hydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)dibenzoylmethane (III).—The foregoing compound (II) (1 g.) and anhydrous potassium carbonate (0·24 g.) in anhydrous pyridine (5 c.c.) were heated under reflux with stirring for 1 hour, cooled, poured into water (100 c.c.), and neutralised with 20% acetic acid. The precipitate was collected, dried, and crystallised from ethanol, giving *2-hydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)dibenzoylmethane* (III) (0·46 g., 46%) as clusters of minute, yellow needles, m. p. 142—143°, $[\alpha]_D^{23}$ −32·2° (*c*, 1·1 in acetone) (Found: C, 59·4; H, 4·8. $C_{29}H_{30}O_{13}$ requires C, 59·4; H, 5·2%). It gave a red-brown colour with ferric chloride.

Reaction of 2-Benzoyloxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone (II) *with Potassium Hydroxide in Pyridine.*—Powdered potassium hydroxide was added to a solution of the acetophenone (II) (1 g.) in anhydrous pyridine (5 c.c.) and, after being shaken at room temperature for 2 hours, the mixture was acidified to pH 6 with 20% acetic acid and then diluted with water (50 c.c.). The precipitate was collected, dried, and crystallised from aqueous ethanol, giving a compound (0·32 g.) as small, pale yellow needles, m. p. 135—136°, $[\alpha]_D^{19}$ −29·2° (*c*, 1·2 in acetone) (Found: C, 59·6; H, 5·5. $C_{29}H_{30}O_{13}$ requires C, 59·4; H, 5·2%). This material, which may be an enol *form* of (III), gave an intense reddish-purple colour with ferric chloride; in very dilute solution the colour was green.

7-(2 : 3 : 4 : 6-Tetra-acetyl β-D-glucosyloxy)flavone (IV).—(*a*) 2-Hydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)dibenzoylmethane (III) (1·75 g.), xylene (50 c.c.), and a trace of toluene-*p*-sulphonic acid were heated under reflux in a Soxhlet apparatus as previously described. After 9 hours, the xylene was removed under diminished pressure and the residue was crystallised (charcoal) from methanol, giving 7-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)flavone (1·1 g., 65%) as long, colourless needles, m. p. 180—181°, $[\alpha]_D^{22}$ −30·8° (*c*, 0·9 in acetone). This m. p. was not depressed when mixed with the material prepared in the following manner.

(*b*) 7-Hydroxyflavone (0·75 g.) and 2 : 3 : 4 : 6-tetra-acetyl α-D-glucosyl bromide (1·4 g.) (Bárczai-Martos and Korösy, *Nature*, 1950, **165**, 369) were dissolved in acetone (5 c.c.), and 5% aqueous sodium hydroxide (2·6 c.c.) was added. After 48 hours at room temperature the mixture was poured into water (100 c.c.), and the precipitate collected, washed repeatedly with sodium carbonate solution and then with water, and dried. Crystallisation from methanol gave the flavone (0·42 g. 33%) as long needles, m. p. 180—181°, $[\alpha]_D^{23}$ −30·7° (*c*, 1·1 in acetone) (Hattori, *loc. cit.*, gives m. p. 183°).

7-β-D-Glucosyloxyflavone.—Both specimens of 7-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)-flavone were hydrolysed as follows. The tetra-acetyl compound (200 mg.) was dissolved in pure chloroform (3 c.c.), and a dilute solution of sodium methoxide in methanol (1·5 c.c.) added. After being kept at 0—5° for 96 hours, the solid was collected, washed with a small amount of water, and crystallised from methanol, giving 7-β-D-glucosyloxyflavone (115 mg., 81%) as long, colourless needles, m. p. 256—257°, $[\alpha]_D^{25}$ −61·5° (*c*, 0·28 in pyridine) [from preparation (*a*)], $[\alpha]_D^{24}$ −63·1° (*c*, 0·46 in pyridine) [from preparation (*b*)]. Hattori (*loc. cit.*) gives m. p. 255°.

4-O-(2 : 3 : 4 : 6-Tetra-acetyl β-D-glucosyl)phloracetophenone.—This compound was prepared by Zemplén and Bognár (*Ber.*, 1942, **75**, 647), but it was not analysed.

To phloracetophene (30 g.) and 2 : 3 : 4 : 6-tetra-acetyl α-D-glucosyl bromide (84 g.) in acetone (150 c.c.) was slowly added 10% aqueous sodium hydroxide (80 c.c.), and after being shaken for 48 hours the solution was poured into iced water (1800 c.c.), methanol (125 c.c.) was added, and the whole extracted with chloroform (some phloracetophenone separated at the interface). The chloroform layer yielded an oil which was crystallised twice from methanol (*ca.* 400 c.c.) at 0—5°, giving *4-O-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyl)phloracetophenone* (7·6 g.) as needles, m. p. 218—219°, $[\alpha]_D^{19}$ −35·4° (*c*, 0·37 in pyridine) (Found: C, 53·0; H, 5·3. $C_{22}H_{26}O_{13}$ requires C, 53·0; H, 5·2%). It gave a faint orange colour with ferric chloride. Zemplén and Bognár (*loc. cit.*) record m. p. 215—216°, $[\alpha]_D^{20}$ −52·7° (in pyridine).

2-Benzoyloxy-6-hydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone.—2 : 6-Dihydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone (7·6 g.) was dissolved in dry pyridine (40 c.c.) and benzoyl chloride (4·3 g.) was slowly added. After 24 hours at room temperature the mixture was poured into iced water, and the sticky solid dissolved in hot ethanol, giving *2-benzoyloxy-6-hydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone* (7·3 g., 68%) as needles, m. p. 153° (Found: C, 55·8; H, 5·3. $C_{29}H_{30}O_{14}.H_2O$ requires C, 56·1; H, 5·2%). It gave no colour with ferric chloride, and in an attempted rearrangement with potassium carbonate in dry pyridine the only isolable product was 2 : 6-dihydroxy-4-(2 : 3 : 4 : 6-tetra-acetyl β-D-glucosyloxy)acetophenone.

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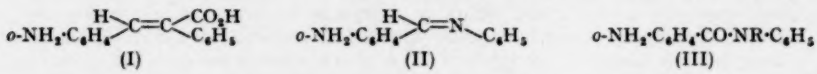
275. *Internuclear Cyclisation. Part III.* An Extension of the Pschorr Phenanthrene Synthesis to the Synthesis of Phenanthridones.*

By R. A. Heacock and D. H. Hey.

Diazonium salts prepared from *o*-amino-*N*-methylbenzanilide have been converted into *N*-methylphenanthridone by eight methods. *o*-Hydroxy-*N*-methylbenzanilide was frequently found as a by-product. Decomposition of the diazonium borofluoride in acetone in presence of copper proved to be a convenient method of preparation of the phenanthridone and this method was also applied successfully to the isomeric *o'*-amino-*N*-methylbenzanilide.

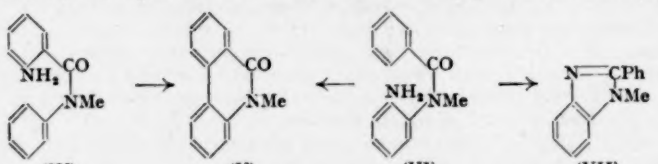
An investigation has been carried out into the extension of the well-known Pschorr reaction for the synthesis of derivatives of phenanthrene to include the synthesis of derivatives of phenanthridine. In order to achieve this object it is necessary to replace the intermediate symmetrical diarylethylene of type (I) by the system (II), but the ease of hydrolysis normally shown by Schiff's bases suggests that more successful results might result from



(I) (II) (III)

the use of the saturated system (III), in which, to eliminate the formation on diazotisation of a triazolone, R should be an alkyl group. The use of compounds of type (III) also eliminates the necessity to consider the geometrical isomerism of the intermediate compound, which in the phenanthrene synthesis is known to be of vital importance. On the other hand, the two positions in the aromatic nuclei between which the new internuclear bond is to be formed are not as near to each other in space as they would be in the appropriate Schiff's base. The successful development of a general method of synthesis in this manner would provide a new and useful route to a variety of substituted phenanthridines, and in addition would enable a new approach to be made to the synthesis of alkaloids of the chelidonine–sanguinarine group. Such an approach was envisaged by Richardson, Robinson, and Seijo (*J.*, 1937, 835), who attempted to apply a Pschorr-type ring closure to the reduction product of the Schiff base prepared from 6-nitropiperonaldehyde and α-naphthylamine, but diazotisation of the amine afforded only a brown tar. The failure of a similar reaction was reported at about the same time by Noller, Denyes, Gates, and Wasley (*J. Amer. Chem. Soc.*, 1937, **59**, 2079).

When this work was started it was known that Pictet and Gonset (*Arch. Sci. phys. nat. Genève*, 1897, **3**, 37) had reported the formation of *N*-methylphenanthridone (V) by heating



(IV) (V) (VI) (VII)

an aqueous solution of the diazonium chloride prepared from *o*-amino-*N*-methylbenzanilide (IV), but no yield was mentioned. In addition, Forrest, Haworth, Pinder, and Stevens (*J.*, 1949, 1311) had reported the formation of *N*-methyl-6 : 7-methylenedioxyphenanthridone in more than 50% yield by heating the diazonium sulphate prepared from 2-amino-*N*-methyl-4 : 5-methylenedioxybenzanilide, although a similar reaction with the *N*-methylbenzo-α-naphthalide failed.

No further examples of the synthesis of the phenanthridine system by this route could be found, but during the course of this work it was learned that Mitsuhashi (*J. Pharm. Soc.*

* Part II, *J.*, 1949, 3172.

Japan, 1943, **63**, 177; *Chem. Abstracts*, 1951, **45**, 628) had obtained *N*-benzylphenanthridone in 54% yield by the action of heat or of copper powder on an aqueous solution of the diazonium salt prepared from *o*-amino-*N*-benzylbenzanilide, and a *N*-benzyl-ethoxy- and a -methoxyphenanthridone were also prepared in similar manner. At the same time Chardonnens and Würmli (*Helv. Chim. Acta*, 1950, **33**, 1338) reported the formation of 1 : 3 : *N*-trimethylphenanthridone in 8% yield from the diazonium chloride prepared from *o*-amino-*N* : 2′ : 4′-trimethylbenzanilide.

As part of a programme of work devised to ascertain the scope and limitations of this synthetic approach to the phenanthridine system, the present communication is limited to a study of the formation of *N*-methylphenanthridone from both *o*-amino- and *o*′-amino-*N*-methylbenzanilide under a variety of experimental conditions with special reference to the yields obtained and the nature of any by-products formed.

The original observation by Pictet and Gonset has been confirmed and, by boiling an aqueous solution of the diazonium sulphate prepared from *o*-amino-*N*-methylbenzanilide, *N*-methylphenanthridone was obtained in 50% yield, together with *o*-hydroxy-*N*-methylbenzanilide in 40% yield. Seven modified procedures were then used, starting in each case with *o*-amino-*N*-methylbenzanilide, and the yields of *N*-methylphenanthridone and the nature of the by-products are shown in the table. The by-products consisted of either the phenol or the dimeride formed by the union of two molecules from which the amino-groups had been eliminated. The maximum yield of *N*-methylphenanthridone (53%) was obtained by the decomposition of the solid diazonium sulphate in acetone in presence of copper (see Hey and Osbond, *J.*, 1949, 3164). Of most interest is the reaction in which the diazonium fluoroborate of *o*-amino-*N*-methylbenzanilide was decomposed in acetone in presence of copper. This reaction, which is clean and easy to carry out, gave *N*-methylphenanthridone in 50% yield. Previous uses of fluoroborate for effecting the union of aryl nuclei have been reported by Nesmejanov and Makarova (*Bull. Acad. Sci. U.R.S.S.*, Classe Sci. Chim., 1947, 213; *Chem. Abstracts*, 1948, **42**, 5440), although in the few examples recorded only very small yields were obtained.

Ring-closure experiments with o-*amino*-N-*methylbenzanilide.*

	Experimental conditions	Yield, %, of *N*-methylphenanthridone	By-products
(*a*)	Heating aq. diazonium sulphate	50	*o*-Hydroxy-*N*-methylbenzanilide (40%)
(*b*)	,, ,, ,, with Cu	50	,, ,, ,, (4%)
(*c*)	,, ,, chloride ,,	29	,, ,, ,, (20%)
(*d*)	Addition of aq. NaOH to diazonium sulphate	11	—
(*e*)	Action of H_3PO_2 on diazonium sulphate in dioxan with Cu	40	Product, m. p. 220°, and dimeride
(*f*)	Solid diazonium sulphate in acetone with Cu	53	*o*-Hydroxy-*N*-methylbenzanilide (3%)
(*g*)	Diazonium fluoroborate ,, ,,	50	Dimeride
(*h*)	,, ,, in boiling light petroleum (b. p. 80—100°)	17	—

The successful use of *o*-amino-*N*-methylbenzanilide (IV) for the synthesis of *N*-methylphenanthridone (V) outlined above suggested that the alternative approach through *o*′-amino-*N*-methylbenzanilide (VI) was worthy of attention. The ease with which monoacyl-*o*-phenylenediamines are known to be converted into benziminazoles indicates that *o*′-amino-*N*-methylbenzanilide might yield 1-methyl-2-phenylbenziminazole (VII), and in the preparation of the base (VI) from the corresponding nitro-compound by means of iron and acetic acid there was evidence that the benziminazole (VII) was in fact formed. Chardonnens and Würmli (*loc. cit.*) have also reported the ready formation of 2-(2 : 4-dimethylphenyl)-1-methylbenziminazole from *o*′-amino-*N* : 2 : 4-trimethylbenzanilide. The base (VI), however, was obtained in quantitative yield on catalytic hydrogenation of the corresponding nitro-compound, and when the diazonium fluoroborate was decomposed under acetone with copper powder, *N*-methylphenanthridone (V) was obtained in 31% yield. This route, however, is somewhat inferior to the former route, since the product is more highly coloured and the yield of phenanthridone is lower.

Experimental

N-*Methyl*-o-*nitrobenzanilide*.—(*a*) Methylaniline (60 c.c.) was slowly added to a boiling ethereal solution of *o*-nitrobenzoyl chloride (from 40 g. of acid). After being boiled under reflux for 4 hours, the suspension was filtered and the precipitate washed with water. The ethereal solution was washed with dilute hydrochloric acid and evaporated. The solid residue was combined with the precipitate, and crystallisation from benzene gave *N*-methyl-*o*-nitrobenzanilide (47 g.) in colourless needles, m. p. 94°.

(*b*) An ethereal solution of *o*-nitrobenzoyl chloride (from 40 g. of acid) was added slowly to a solution of methylaniline (25·6 g.) in pyridine (60 c.c.) The ether was evaporated and the clear pyridine solution was boiled for 5 minutes, cooled, and poured into water. Crystallisation from benzene (charcoal) of the solid which separated gave the anilide (45 g.) in colourless needles, m. p. 94°. Pictet and Gonset (*loc. cit.*) recorded m. p. 94·5° for this compound prepared by the Schotten–Baumann reaction (no yield quoted).

o-*Amino*-N-*methylbenzanilide*.—A suspension of iron filings (80 g.) in 5% aqueous acetic acid (100 c.c.) was heated on a steam-bath, with stirring, until no more hydrogen was evolved. *N*-Methyl-*o*-nitrobenzanilide (35 g.) was slowly added, and the mixture was stirred on the steam-bath for 1 hour. The solution was neutralised with aqueous sodium carbonate, and charcoal added to assist filtration. After filtration, both residue and filtrate were repeatedly extracted with hot benzene. The combined benzene extracts were concentrated, and *o*-amino-*N*-methylbenzanilide (26 g.) separated in white needles, m. p. 126—127°. Pictet and Gonset (*loc. cit.*) carried out the reduction with ammonium sulphide and recorded m. p. 127° but no yield. When the base was (*a*) heated with an excess of acetic anhydride for 30 minutes, or (*b*) left overnight at room temperature with acetic acid, acetic anhydride, and a few drops of concentrated sulphuric acid, only *N*-acetylanthranilic acid was isolated from the product. Acetyl chloride (5 c.c.) was slowly added to a stirred solution of *o*-amino-*N*-methylbenzanilide (6·2 g.) in pyridine (20 c.c.) at 0°. A vigorous reaction took place and the mixture was poured into a large excess of ice-water. The white solid which separated was recrystallised from benzene–light petroleum (b. p. 60—80°) and **o-*acetamido*-N-*methylbenzanilide*** (6·1 g.) separated in white cubic crystals, m. p. 124—125° (Found: C, 72·1; H, 5·8. $C_{16}H_{16}O_2N_2$ requires C, 71·6; H, 6·0%). Admixture with the starting material (m. p. 126—127°) resulted in a strong depression in m. p.

N-*Methylbenzanilide*-o-*diazonium Fluoroborate*.—*o*-Amino-*N*-methylbenzanilide (2·5 g.) was dissolved in concentrated sulphuric acid (20 c.c.) and water (40 c.c.) by warming, and after this had been cooled to 0° a solution of sodium nitrite (1 g.) in water (10 c.c.) was added. After being stirred for 1 hour at 0° the pale yellow-green solution was filtered, and a solution of sodium fluoroborate (5 g.) in water (20 c.c.) was slowly added to a stirred solution at 0°. The fluoroborate separated as a pale yellow solid (7·5 g.), m. p. 122·5° (decomp.), which was collected in a sintered-glass crucible and washed with a little ice-cold water. Purification was effected by dissolving the compound in boiling " AnalaR " acetone, quickly cooling the solution in an ice–salt freezing mixture, and precipitating the diazonium salt by addition of light petroleum (b. p. 40—60°). **N-*Methylbenzanilide*-o-*diazonium fluoroborate*** was obtained in very pale yellow needles, m. p. 125° (decomp.) (Found: C, 51·5; H, 4·0; N, 12·8. $C_{14}H_{12}ON_2BF_4$ requires C, 51·7; H, 3·7; N, 12·9%).

Preparation of **N-*Methylphenanthridone*.**—(*a*) *o*-Amino-*N*-methylbenzanilide (2·2 g.) was diazotised as described above in a mixture of concentrated sulphuric acid (5 c.c.) and water (100 c.c.) by addition at 0° of sodium nitrite (0·8 g.) in water (10 c.c.). The filtered solution was gently warmed on a water-bath to 70°, whereat decomposition commenced. The reaction was complete after about 1½ hours and much tar was formed. The mixture was extracted with chloroform, and the chloroform solution was repeatedly extracted with 10% aqueous sodium hydroxide to remove phenolic substances. Evaporation of the dried (Na_2SO_4) neutral extract left a light brown solid (1·3 g.), m. p. 96—98°. Recrystallisation from benzene–light petroleum (b. p. 60—80°) with charcoal gave *N*-methylphenanthridone (0·98 g.) in white needles, m. p. 104—105° (Found: C, 80·0; H, 5·0. Calc. for $C_{14}H_{11}ON$: C, 80·3; H, 5·2%). Pictet and Gonset (*loc. cit.*) quoted no yield but gave m. p. 109° for this compound. Acidification of the sodium hydroxide washings and extraction with ether gave a brown solid (0·96 g.), m. p. 102—108°, which on recrystallisation from aqueous alcohol (charcoal) afforded *o*-hydroxy-*N*-methylbenzanilide (0·8 g.), m. p. 112—113°, both alone and on admixture with an authentic specimen. Pictet and Gonset (*loc. cit.*) did not record the isolation of any phenolic compound.

(*b*) *o*-Amino-*N*-methylbenzanilide (3 g.) was diazotised as described above in a mixture of

concentrated sulphuric acid (5 c.c.) and water (100 c.c.) by addition at 0° of sodium nitrite (1 g.) in water (10 c.c.). To the filtered solution copper powder * (3 g.) was slowly added, and nitrogen was evolved in the cold. The solution was stirred at room temperature for 24 hours, and then boiled. The resulting suspension was filtered, and both filtrate and residue were repeatedly extracted with hot chloroform. The chloroform solution was washed with 10% aqueous sodium hydroxide and concentrated, as in (*a*). A brown tar (2·6 g.) was obtained. Purification was effected by dissolving the tar in benzene–light petroleum (b. p. 60—80°) (4 : 1), adsorption on an alumina column (20 × 2 cm.), and washing the column with the same solvent. *N*-Methylphenanthridone (1·4 g.) was obtained in white needles, m. p. 109° [cf. reaction (*a*)]. When this was admixed with the product obtained from reaction (*a*) no depression in m. p. was observed, and on seeding of a solution of the compound, m. p. 105°, with a crystal of m. p. 109°, the resulting product had m. p. 108—109°. Further washing of the column with benzene and ether gave brown viscous oils of unidentified composition. The alkaline extract, treated as described above, gave a brown crystalline solid (0·05 g.) which on recrystallisation from aqueous alcohol afforded *o*-hydroxy-*N*-methylbenzanilide (0·03 g.) in white needles, m. p. 112°.

(*c*) *o*-Amino-*N*-methylbenzanilide (3 g.) was diazotised in a mixture of concentrated hydrochloric acid (5 c.c.) and water (100 c.c.) by addition at 0° of sodium nitrite (1 g.) in water (10 c.c.). To the filtered solution copper powder (3 g.) was slowly added and nitrogen was evolved. The suspension was stirred for 24 hours and then boiled. The product was worked up as described under reaction (*b*). The neutral extract yielded a brown solid (1·6 g.), m. p. 95—100°, which on recrystallisation from benzene–light petroleum (b. p. 60—80°) with charcoal gave *N*-methylphenanthridone (0·8 g.) in colourless needles, m. p. 105°. The alkaline extract yielded a brown solid, which on recrystallisation from aqueous alcohol (charcoal) gave *o*-hydroxy-*N*-methylbenzanilide (0·6 g.), m. p. 111—112°.

(*d*) *o*-Amino-*N*-methylbenzanilide (2 g.) was diazotised as described above in a mixture of concentrated sulphuric acid (5 c.c.) and water (50 c.c.) by the addition at 0° of sodium nitrite (0·8 g.) in water (10 c.c.) Aqueous sodium hydroxide (10%) was added dropwise to the filtered diazonium solution with stirring at 0° until the solution was just alkaline to phenolphthalein. The pale yellow solution became cloudy, but there was no change in colour or evolution of nitrogen. The solution was stirred at room temperature for 3 days, during which the colour of the suspension changed from pale yellow to deep orange and nitrogen was slowly evolved. The reaction was completed by warming to 70° on a water-bath, with stirring, for a further 3 hours. The solution and suspended tar were then extracted with chloroform. Evaporation of the chloroform extract left a red-brown tar (0·8 g.), which was dissolved in benzene–light petroleum (b. p. 60—80°) (2 : 1) and adsorbed on an alumina column (25 × 2 cm.). When the column was washed with benzene–light petroleum (b. p. 60—80°) (4 : 1) (500 c.c.) a pale orange solid (0·25 g.), m. p. 100—108°, was obtained. Recrystallisation from light petroleum (b. p. 80—100°) with charcoal gave *N*-methylphenanthridone (0·2 g.), m. p. 109°, in colourless needles. Further washing of the column with benzene and with ether gave orange and red vitreous substances of unidentified composition. Acidification of the original alkaline-soluble reaction product and extraction with chloroform gave a brown tar from which no identifiable products were obtained.

(*e*) A solution of *o*-amino-*N*-methylbenzanilide (2 g.) in a mixture of dioxan (40 c.c.) and concentrated sulphuric acid (3 c.c.) was diazotised by slow addition of amyl nitrite (4 c.c.) at room temperature. The solution was stirred at room temperature for 2 hours to complete the reaction. The bright yellow solution was added dropwise to a stirred suspension of copper (4 g.) in a solution of sodium hypophosphite (18 g.) in water (20 c.c.) (cf. Cassaday and Bogert, *J. Amer. Chem. Soc.*, **1939**, **61**, 2461, 3058). The mixture was stirred at 70—80° for 1 hour. The cooled suspension was filtered and both the filtrate and the residue were extracted with hot chloroform, and the chloroform extracts were washed with 10% aqueous sodium hydroxide. Concentration of the neutral extract left a red-brown solid (1·1 g.), which was dissolved in benzene–light petroleum (b. p. 60—80°) and adsorbed on an alumina column (24 × 2 cm.). On washing of the column with benzene–light petroleum (4 : 1) (600 c.c.) a white solid (0·9 g.), m. p. 102—104°, was obtained, which on crystallisation from light petroleum (b. p. 80—100°) yielded *N*-methylphenanthridone (0·75 g.), m. p. 109°, in colourless needles. On washing of the column with benzene–ether (1 : 1) a pale orange solid (0·2 g.), m. p. 210—220°, was obtained, which on recrystallisation from methanol gave crude 2 : 2′-bis-*N*-methylbenzamidodiphenyl (0·1 g.) in pale yellow prisms, m. p. 240—242° [cf. reaction (*g*)]. Further washing of the column

* In all the reactions described in this paper the copper powder was prepared by precipitation from aqueous copper sulphate with zinc dust.

with the same solvent gave only orange glassy material of unidentified composition. Acidification of the alkaline washings gave a pale brown solid (1 g.), which on recrystallisation from methanol gave a product, m. p. 220° (Found: C, 70·5; H, 5·2%).

(*f*) A solution of *o*-amino-*N*-methylbenzanilide (2 g.) in glacial acetic acid (20 c.c.) was cooled to 0° with vigorous stirring and diazotised by addition of sodium nitrite (2 g.) in concentrated sulphuric acid (10 c.c.) (cf. Hodgson and Mahadevan, *J.*, 1947, 325). The solution was allowed to warm to room temperature with stirring to complete the reaction, and dry ether was then added. The ethereal layer was decanted and the diazonium sulphate, obtained as a viscous gum, was dissolved in " AnalaR " acetone. Some sodium hydrogen sulphate which had separated was filtered off. Copper powder (3 g.) was added to the acetone solution and an immediate vigorous evolution of nitrogen took place. The reaction was complete in a few minutes. The acetone solution was filtered into water and the copper powder was extracted with hot acetone and washed with boiling water. The whole aqueous-acetone solution was extracted with chloroform, and the chloroform solution washed with 10% aqueous sodium hydroxide. Evaporation of the neutral chloroform extract yielded a brown tar (1·7 g.), which was dissolved in benzene–light petroleum (b. p. 60—80°) (5 : 1) and adsorbed on an alumina column (25 × 2 cm.). On washing of the column with the same solvent (800 c.c.) a pale yellow solid (1·15 g.), m. p. 99—104°, was obtained. Recrystallisation from light petroleum (b. p. 80—100°) gave *N*-methylphenanthridone (0·97 g.), m. p. 105° [cf. reaction (*b*)] (Found: C, 80·3; H, 5·3. Calc. for $C_{14}H_{11}ON$: C, 80·3; H, 5·2%). Further washing of the column with benzene and benzene–ether mixtures gave a series of unidentifiable brown tars. The alkaline extract on acidification yielded a brown solid (0·08 g.), which on recrystallisation from aqueous alcohol (charcoal) gave *o*-hydroxy-*N*-methylbenzanilide (0·05 g.), m. p. 110—112°.

(*g*) Dry *N*-methylbenzanilide-*o*-diazonium borofluoride (2·5 g.), prepared as described above, was suspended in " AnalaR " acetone (50 c.c.), and on the addition of copper powder (3 g.) a vigorous evolution of nitrogen occurred. The reaction was complete within a few minutes and the solution was then filtered into an excess of cold water. The copper powder was washed with boiling water and hot acetone, and the whole aqueous-acetone solution extracted with chloroform. The chloroform extract was washed with 10% aqueous sodium hydroxide. Concentration of the neutral extract gave a light brown solid (2·0 g.), which was dissolved in benzene–light petroleum (b. p. 60—80°) (1 : 1) and adsorbed on an alumina column (25 × 2 cm.). Washing of the column with benzene–light petroleum (b. p. 60—80°) (3 : 1) (500 c.c.) and (9 : 1) (500 c.c.) gave white and pale pink solids (0·9 g. and 0·1 g.), m. p. 96—99° and 90—100°, respectively. Recrystallisation of these combined fractions from light petroleum (b. p. 60—80°) with charcoal gave *N*-methylphenanthridone (0·84 g.), m. p. 105°. Further washing of the column with benzene (500 c.c.) and benzene–ether (500 c.c.) gave a yellow solid (0·9 g.), m. p. 203—210°. Recrystallisation from benzene and then from alcohol gave 2 : 2′-*bis*-*N*-*methylbenzamidodiphenyl* (0·4 g.) in colourless prisms, m. p. 248—249° (Found: C, 80·1; H, 5·8%; *M*, 402. $C_{28}H_{24}O_2N_2$ requires C, 80·0; H, 5·7%; *M*, 420). Acidification and subsequent extraction of the alkaline washing gave only a trace of a black tar.

(*h*) A suspension of *N*-methylbenzanilide-*o*-diazonium borofluoride (3 g.) in sodium-dried light petroleum (b. p. 80—100°) (150 c.c.) was boiled under reflux for 12 hours. A large amount of a dark red insoluble tar was formed from which the solution was decanted. The tar was extracted with benzene and the benzene extract and light petroleum solution were combined and concentrated. *N*-Methylphenanthridone (0·32 g.) was obtained in colourless needles, m. p. 109°.

N-*Methyl*-o′-*nitrobenzanilide*.—(*a*) A solution of *o*′-nitrobenzanilide (30 g.), prepared by the method of Fischer and Römer (*J. pr. Chem.*, 1906, **73**, 432), in acetone (30 c.c.) with potassium hydroxide (30 g.) was boiled under reflux while methyl sulphate (50 c.c.) was slowly added. When the vigorous reaction had subsided the mixture was cooled and added to an excess of ice-cold ammonia (*d* 0·88). The yellow oil, which separated, solidified. Recrystallisation from aqueous alcohol or from benzene–light petroleum (b. p. 60—80°) gave *N-methyl-o′-nitrobenzanilide* (18·4 g.) in pale yellow plates, m. p. 80—81° (Found: C, 65·6; H, 4·6. $C_{14}H_{12}O_3N_2$ requires C, 65·6; H, 4·7%).

(*b*) *N*-Methyl-*o*-nitroaniline (3·3 g.), prepared by the method of Usherwood and Whiteley (*J.*, 1923, **123**, 1084), and benzoyl chloride (2·8 c.c.) were heated on the steam-bath for one hour. Trituration of the product with light petroleum (b. p. 40—60°) gave the crude benzoyl derivative, m. p. 75—78°. Recrystallisation from aqueous alcohol gave *N*-methyl-*o*′-nitrobenzanilide (3·2 g.) in pale yellow plates, m. p. 81°.

o′-*Amino*-N-*methylbenzanilide*.—A solution of *N*-methyl-*o*′-nitrobenzanilide (7 g.) in ethyl

alcohol (200 c.c.) and a suspension of Raney nickel (7 g.) in ethyl alcohol was shaken with hydrogen at atmospheric pressure for 1½ hours. When 1800 c.c. of hydrogen had been absorbed the suspension was filtered, and the filtrate concentrated under reduced pressure. The resulting white solid was crystallised from dry benzene. *o'-Amino-N-methylbenzanilide* (5·6 g.) was obtained in needles, m. p. 125—126° (Found: C, 74·5; H, 6·1. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2%).

Conversion of o'-Amino-N-methylbenzanilide into N-Methylphenanthridone.—*o'*-Amino-*N*-methylbenzanilide (2·5 g.) in sulphuric acid (20 c.c.) and water (60 c.c.) was diazotised at 0—5° with sodium nitrite (2 g.) in water (10 c.c.). To the filtered solution of the diazonium sulphate at 0°, a solution of sodium fluoroborate (5 g.) in water (10 c.c.) was slowly added with stirring. After ½ hour the solid diazonium fluoroborate was filtered off and dried *in vacuo* (3·7 g.). Copper powder (3 g.) was added to a suspension of the borofluoride in "AnalaR" acetone (50 c.c.) and an immediate evolution of nitrogen ensued. After ½ hour the suspension was filtered into cold water and the residue was extracted with hot acetone and boiling water. The combined washings and filtrate were extracted with chloroform. After being washed with aqueous sodium hydroxide, the chloroform was evaporated and a brown tar (2·1 g.) remained. A solution in benzene–light petroleum (b. p. 60—80°) (3 : 1) was adsorbed on an alumina column (20 × 2 cm.). Elution with the same solvent gave *N*-methylphenanthridone (0·71 g.) in colourless needles, m. p. 105°.

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276. *Internuclear Cyclisation. Part IV.* The Preparation of o-Amino-α-benzylcinnamic Acid.*

By A. Ashdown and D. H. Hey.

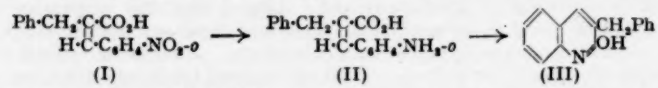
o-Amino-α-benzylcinnamic acid, prepared by the action of *o*-nitrobenzaldehyde on β-phenylpropionic acid and subsequent reduction, readily underwent cyclodehydration to give 3-benzylcarbostyril.

The most familiar examples of internuclear cyclisation are to be found in the Pschorr phenanthrene synthesis, in which the formation of the new internuclear bond results in the creation of a six-membered ring. In addition, there are many closely related reactions in which a new five-membered ring is formed, as in the synthesis of fluorene, fluorenone, dibenzofuran, dibenzothiophen, and carbazole derivatives (see Saunders, "The Aromatic Diazo Compounds," London, 1949, p. 258—265), by reactions which involve diazotisation and the complete elimination of the nitrogen atoms. We were therefore interested in whether analogous reactions could be applied to the formation of a new seven-membered ring, and in the first instance we considered the synthesis of a dibenzo*cyclo*heptatriene. An unsuccessful attempt to synthesise a dibenzo*cyclo*octatetraene on similar lines has been reported by Bachman and Hoaglin (*J. Org. Chem.*, 1943, **8**, 300).

In an attempt to follow as closely as possible the established Pschorr phenanthrene synthesis attention was directed to the preparation of *o*-amino-α-benzylcinnamic acid and an examination of its properties, although it was recognised that this method of approach presented a number of special difficulties. In the first place it might not be possible to control the stereochemical configuration of the intermediate *o*-amino-α-benzylcinnamic acid in such a way that the two aromatic rings are in the *cis*-configuration, as in *o*-amino-α-phenylcinnamic acid, and secondly it is clear from scale models that the nuclear positions between which the new bond is to be formed are much less favourably placed even in the required *cis*-configuration than they are in the phenanthrene synthesis. Again, the preparative methods for α-benzylcinnamic acids are known to be much less satisfactory than the corresponding methods for α-phenylcinnamic acids because of the comparatively low reactivity of β-phenylpropionic acid in the Perkin reaction (cf. Rupe and Häussler, *Annalen*, 1913, **395**, 106; Shoppee, *J.*, 1930, 968). The α-benzylcinnamic acids also contain a three-carbon tautomeric system.

* Part III, preceding paper.

When *o*-nitrobenzaldehyde was heated with β-phenylpropionic acid and acetic anhydride in the presence of litharge (cf. Kuhn and Winterstein, *Helv. Chim. Acta*, 1928, **11**, 87) the acidic product consisted mainly of unchanged β-phenylpropionic acid and *o*-nitrocinnamic acid, but in addition α-benzyl-*o*-nitrocinnamic acid (I) was obtained in small yield. In an attempt to eliminate the formation of *o*-nitrocinnamic acid the acetic anhydride was replaced by β-phenylpropionic anhydride, but in this instance the acidic product appeared to consist solely of β-phenylpropionic acid. Reduction of α-benzyl-*o*-nitrocinnamic acid (I) with ammonia and ferrous sulphate or with ammonium sulphide gave *o*-amino-α-benzylcinnamic acid (II), which, however, was relatively unstable and readily underwent cyclodehydration to give 3-benzylcarbostyril (III). For purposes of comparison an authentic specimen of (III) was prepared by heating 3-benzylquinoline with potassium hydroxide



(I) (II) (III)

at 350°. It would thus appear that in these preparations the resulting *o*-amino-α-benzylcinnamic acid has the carboxyl group and the *o*-aminophenyl group in the unwanted *cis*-configuration. The configuration of the α-benzyl-*o*-nitrocinnamic acid is not known, but rearrangement may have occurred during the reduction of the nitro-group as in the analogous example quoted by Bachman and Hoaglin (*loc. cit.*, p. 306).

Experimental

β-Phenylpropionic Anhydride.—A mixture of β-phenylpropionic acid (18 g.) and acetic anhydride (60 c.c.) was boiled under reflux in a Claisen flask fitted with a cold finger, containing ethylene dibromide in the first neck, and a thermometer in the second. With the bath temperature at 180° acetic acid rapidly distilled at 120°. As the rate of distillation slowed down the temperature dropped to 40°. After 5 hours the excess of acetic anhydride was removed by distillation, and *β-phenylpropionic anhydride* (12·5 g.) was collected at 165—167°/0·25 mm. as a clear liquid (Found: C, 76·0; H, 6·3. $C_{18}H_{18}O_3$ requires C, 76·5; H, 6·4%).

α-Benzyl-o-nitrocinnamic Acid.—(*a*) A mixture of β-phenylpropionic acid (10 g.), *o*-nitrobenzaldehyde (10 g.), acetic anhydride (17 g.), and litharge (7·5 g.) was heated under reflux for 4 hours. The mixture was poured into water (300 c.c.) which was then boiled. The supernatant liquid was decanted from the red oil, which had separated on cooling, and the oil was extracted with boiling aqueous sodium carbonate. Acidification gave a pale brown precipitate consisting of β-phenylpropionic acid, *o*-nitrocinnamic acid, and α-benzyl-*o*-nitrocinnamic acid. By fractional crystallisation from aqueous alcohol *α-benzyl-o-nitrocinnamic acid* (0·78 g.) was obtained as the most soluble acid constituent; it separated in diamond-shaped crystals, m. p. 194—196° (Found: C, 67·8; H, 4·75; N, 4·9. $C_{16}H_{13}O_4N$ requires C, 67·8; H, 4·6; N, 4·95%). (*b*) In a subsequent experiment, in which a mixture of β-phenylpropionic acid (12·5 g.), β-phenylpropionic anhydride (12·5 g.), *o*-nitrobenzaldehyde (12·5 g.), and litharge (9·2 g.) was heated at 150° for 4 hours, only β-phenylpropionic acid was isolated from the acidic product, which was free from nitrogenous acids.

Reduction of α-Benzyl-o-nitrocinnamic Acid.—(*a*) A solution of α-benzyl-*o*-nitrocinnamic acid (1·5 g.) in excess of aqueous ammonia was added to a boiling solution of ferrous sulphate (10 g.) in water (100 c.c.) with vigorous stirring. Ammonia (90 c.c.; *d* 0·88) was slowly added while the mixture was boiled under reflux for 20 minutes. The hot mixture was filtered and neutralised with hydrochloric acid. Recrystallisation of the white precipitate from alcohol gave products of variable melting point, which indicated that the amine was being readily converted into 3-benzylcarbostyril by loss of water. The *3-benzylcarbostyril* (0·12 g.) was finally obtained in small needles, m. p. 193—194° (Found: C, 81·6; H, 5·6; N, 5·9. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·5; N, 6·0%). (*b*) Hydrogen sulphide was passed for 6 hours into a solution of α-benzyl-*o*-nitrocinnamic acid (0·5 g.) in ammonia solution (25 c.c.; *d* 0·88) and water (50 c.c.) at 0°. After the excess of ammonia and hydrogen sulphide had been boiled off, the hot solution was filtered. Addition of acetic acid gave a yellow precipitate which was dissolved in excess of dilute hydrochloric acid, and the hot solution again filtered to remove sulphur. Careful addition of dilute ammonia solution precipitated *o-amino-α-benzylcinnamic acid* (0·38 g.), which separated from alcohol, with one molecule of water of crystallisation, in small needles, m. p. 182—183° (Found: C, 69·8; H, 6·2; N, 5·4. $C_{16}H_{15}O_2N,H_2O$ requires C, 70·3; H,

6·3; N, 5·2%). The amino-group could be diazotised and the product coupled with alkaline β-naphthol. Subsequent repeated recrystallisation of the amine resulted in its gradual conversion into 3-benzylcarbostyril.

3-Benzylcarbostyril.—A mixture of 3-benzylquinoline (1 g.), prepared by Borsche's method (*Annalen*, **1937**, **532**, 141), and potassium hydroxide (1 g.), which had been dried at 350°/0·05 mm. for an hour, was heated in a copper tube at 350° for 3 hours. The cooled product was extracted with water, and the aqueous extract made neutral with hydrochloric acid. The resulting brown precipitate (0·01 g.) was dissolved in alcohol and the solution boiled with charcoal. 3-Benzylcarbostyril separated from the filtered solution in small needles, m. p. 193—194° undepressed on admixture with the compound obtained as above from *o*-amino-α-benzylcinnamic acid.

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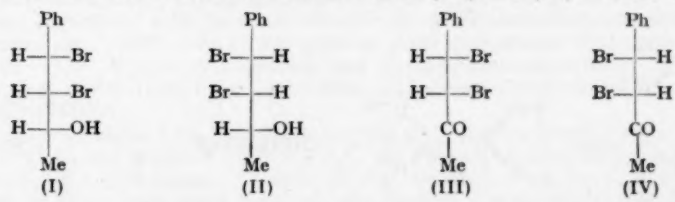
277. *The Addition of Acyl Hypobromites to Styrene.*

By D. C. ABBOTT and C. L. ARCUS.

Acyl hypobromites, prepared by the reaction of bromine with silver (+)- and (−)-2-ethylhexanoates, add to styrene to form (+)- and (−)-2-bromo-1-phenylethyl 2-ethylhexanoates,* hydrolysis of which yields optically inactive phenylglycol; it is concluded that racemisation does not occur during hydrolysis and, therefore, that the two configurations at the new asymmetric centre are formed in equal quantities.

Acetyl hypobromite by addition to styrene forms 2-bromo-1-phenylethyl acetate.

BY the addition of bromine to (+)-4-phenylbut-3-en-2-ol, Kenyon and Partridge (*J.*, 1936, 1313) obtained a mixture of unequal quantities of the dibromo-alcohols (I) and (II). Only two of the four possible isomers were formed and they are here represented as the products of *trans*-addition to the *trans*-alcohol. Oxidation of the mixed dibromo-alcohols gave an optically-active mixture of the enantiomeric ketones (III) and (IV). These reactions, in



which two new centres of asymmetry are formed with one configuration preponderating and the original centre is subsequently rendered symmetrical, constitute a (partial) asymmetric synthesis.

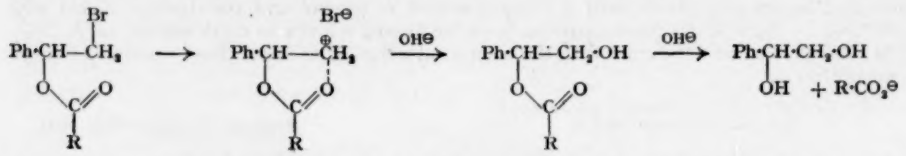
The asymmetric synthesis just described was effected by the addition of a symmetrical reagent to an optically active compound containing a double bond, and it was decided to attempt an asymmetric synthesis in the reverse way, by adding an optically active reagent to a symmetrical olefin. Several examples of the addition of acyl hypobromites (formed by the reaction of two equivalents of bromine with the silver salt of the acid) to *cyclo*hexene have been recorded (Bockemüller and Hoffmann, *Annalen*, 1935, **519**, 165; Uschakow and Tschistow, *Ber.*, 1935, **68**, 824)—they give the 2-bromo*cyclo*hexyl esters—and the acyl hypobromite derived from an optically active acid appeared to be a possible reagent for an asymmetric synthesis. Styrene used was because only one new asymmetric centre is formed and, after removal of the acyl group, diastereoisomerism cannot occur.

Silver (+)-2-ethylhexanoate * and bromine were allowed to react in carbon tetrachloride at −15°; the colour disappeared after 10 minutes; reaction of styrene with the solution

* Geneva numbering, $CO_2H=1$.

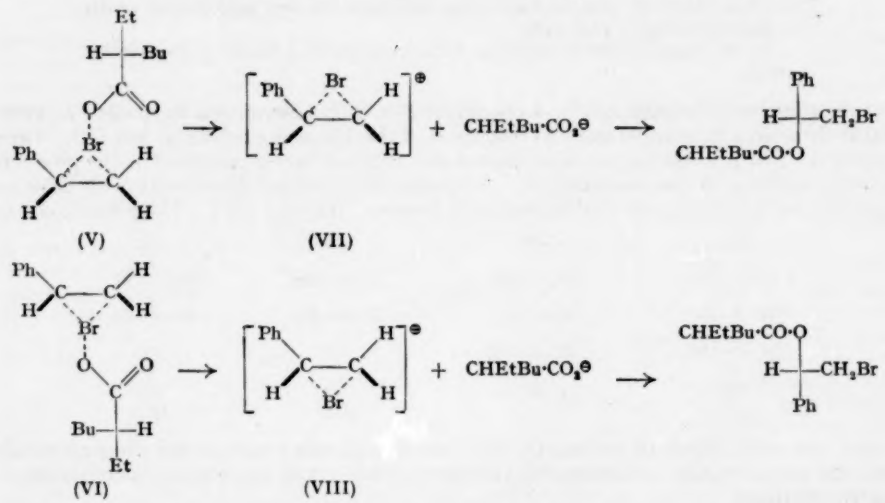
then gave (+)-2-bromo-1-phenylethyl 2-ethylhexanoate. Alkaline hydrolysis of this ester yielded (±)-phenylglycol. Silver (−)-2-ethylhexanoate similarly gave the (−)-ester and then (±)-phenylglycol.

The most probable course for the hydrolysis is considered, from the results of Winstein and Buckles for the reaction of 2-acetoxy-3-bromobutanes with silver acetate (*J. Amer. Chem. Soc.*, 1942, **64**, 2780), to be :



the last stage occurring by normal alkaline hydrolysis with acyl–oxygen fission. The bonding of the new asymmetric centre remains unchanged on this mechanism. It is possible, in the second stage of reaction, for the hydroxyl ion to attach itself to this centre, yielding 2-hydroxy-2-phenylethyl 2-ethylhexanoate; this would result in inversion but not in racemisation.

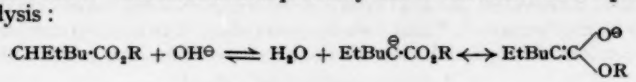
It is concluded that racemisation did not occur during the hydrolysis of the bromo-ester to phenylglycol and, therefore, that addition occurred symmetrically yielding the intermediates (VII) and (VIII) in equal quantities. The result implies that there is no appreci-



able difference in the rates of formation of the diastereoisomeric critical complexes (V) and (VI).

Acetyl hypobromite, prepared from silver acetate and bromine, gave with styrene an ester, the physical constants of which agreed closely with those of the 2-bromo-1-phenylethyl acetate prepared by Marvel and Moon (*J. Amer. Chem. Soc.*, 1940, **62**, 40) by the acetylation of styrene bromohydrin, and it is inferred that the 2-ethylhexanoates above are also 2-bromo-1-phenylethyl esters.

The (+)- and (−)-2-ethylhexanoic acid recovered from the hydrolyses were respectively 36 and 40% racemised. Racemisation is probably due to the removal of a proton from $C_{(\alpha)}$ during hydrolysis :



Kenyon and Young (*J.*, 1940, 216) found that (−)-ethyl 2-ethylhexanoate, when heated with one equivalent of sodium ethoxide in alcohol for 20 minutes at 80°, was completely racemised.

Experimental

Carbon tetrachloride was kept over calcium chloride and distilled, then dried with, and distilled from, phosphoric oxide; it was kept over the latter.

Bromine was twice shaken with an equal volume of concentrated sulphuric acid and distilled from phosphoric oxide.

Styrene was kept over sodium sulphate and was distilled, a little quinol having been added, immediately before use.

2-Ethylhexanoic acid was prepared and resolved by the method of Kenyon and Platt (*J.*, 1939, 633).

(+)-2-Ethylhexanoic acid (19·8 g.) was added to warm N-sodium hydroxide (130 ml.) and the solution titrated with further aqueous sodium hydroxide until just alkaline to phenolphthalein. This solution was added dropwise with stirring to a warm solution of silver nitrate (23·4 g.) in water (100 ml.); the precipitated silver (+)-2-ethylhexanoate was washed with water, acetone, and ether. It was dried ($CaCl_2$) in a vacuum, finely ground, and dried again (P_2O_5) in a vacuum; the yield was 34·2 g. (99%). Silver (−)-2-ethylhexanoate and silver acetate were prepared similarly.

Addition Reactions.—A suspension of the silver salt (15·2 g.) of (+)-2-ethylhexanoic acid (b. p. 118—121°/15 mm., α^{25}_{5893} +15·07°, *l* 2·0; 93% optically pure) in carbon tetrachloride (150 ml.) was cooled, in ice–salt at between −20° and −10°, and vigorously stirred while a solution of bromine (9·5 g.) in carbon tetrachloride (25 ml.) was added. After 10 minutes all colour of bromine had disappeared, and styrene (6·3 g.) in carbon tetrachloride (25 ml.) was added; stirring and cooling were continued for 30 minutes. The reaction mixture was allowed to attain room temperature and filtered through sintered-glass. The filtrate was twice washed with aqueous sodium hydrogen carbonate (25 ml., 20%) and dried (Na_2SO_4). The carbon tetrachloride was distilled and unchanged styrene removed at 100°/15 mm. The residue on distillation yielded two fractions: (i), b. p. 110—120°/1 mm., which solidified and, after recrystallisation from aqueous alcohol, gave styrene dibromide (0·9 g.), plates, m. p. 73° alone and when mixed with an authentic specimen of m. p. 73°; and (ii), (+)-2-*bromo*-1-*phenylethyl* 2-*ethylhexanoate* (12·0 g., 60%), b. p. 152—156°/1·5 mm., n^{25}_D 1·5081, α^{18}_{5893} +0·88° (*l* 0·5) (Found: C, 58·9; H, 7·0; Br, 24·7. $C_{16}H_{23}O_2Br$ requires C, 58·7; H, 7·1; Br, 24·4%).

A similar experiment with the silver salt (14·8 g.) of (−)-2-ethylhexanoic acid (b. p. 122—125°/17 mm.; α^{15}_{5893} −2·95°, *l* 0·5; 75% optically pure) gave styrene dibromide (1·9 g.), m. p. 69—71°, m. p. 73° after recrystallisation, and (−)-2-bromo-1-phenylethyl 2-ethylhexanoate (6·6 g., 35%), b. p. 150—154°/1 mm., n^{25}_D 1·5080, α^{17}_{5893} −0·61° (*l* 0·5) (Found: C, 58·8; H, 7·3; Br, 24·8%).

A similar experiment with silver acetate (33·4 g.) yielded 2-bromo-1-phenylethyl acetate (29·1 g., 60%) having b. p. 100—104°/0·6 mm., n^{25}_D 1·5391 and, after redistillation, b. p. 98—100°/0·3 mm., n^{25}_D 1·5389 (Found: C, 49·2; H, 4·6; Br, 33·3. Calc. for $C_{10}H_{11}O_2Br$: C, 49·4; H, 4·6; Br, 32·8%). Marvel and Moon (*loc. cit.*) record b. p. 105—107°/3 mm., n^{20}_D 1·5380.

Hydrolyses.—2-Bromo-1-phenylethyl acetate (1·8 g.) was heated under reflux for 3 hours with N-sodium hydroxide (20 ml.). The cooled solution was saturated with potassium carbonate and extracted with ether. The extract was dried (Na_2SO_4) and ligroin (b. p. 100—120°) added, whereupon there separated phenylglycol (0·6 g., 60%), m. p. 64—65° Found: C, 69·4; H, 7·4. Calc. for $C_8H_{10}O_2$: C, 69·5; H, 7·3%); its dibenzoate had m. p. 93—94°. Milas and Sussman (*J. Amer. Chem. Soc.*, 1937, **59**, 2346) record m. p. 65—66° and m. p. 92—93° for phenylglycol and the dibenzoate.

(+)-2-Bromo-1-phenylethyl 2-ethylhexanoate (3·3 g.) was similarly hydrolysed for 10 hours with 3N-sodium hydroxide (40 ml.). The ethereal extract (dried with K_2CO_3) was optically inactive (*c* 5, *l* 2·0) and yielded phenylglycol (0·9 g., 65%), m. p. 63—65° and, after recrystallisation from ether–ligroin, m. p. 64·5—65·5°. The aqueous solution was acidified with hydrochloric acid and extracted with ether. The extract was dried (Na_2SO_4) and distilled, and yielded (+)-2-ethylhexanoic acid (1·2 g., 80%), b. p. 223—225°, α^{17}_{5893} +2·40° (*l* 0·5), whence the acid had undergone 36% racemisation.

From a similar hydrolysis of (−)-2-bromo-1-phenylethyl 2-ethylhexanoate (3·3 g.) there was obtained an ethereal extract having α^{14}_{5893} −0·02° (*c* 5·9, *l* 2·0) which gave phenylglycol (1·0 g., 74%), m. p. 60—62°, m. p. 64—65° and optically inactive in ether (*c* 3·7, *l* 2·0) after recrystallis-

ation. From the aqueous solution there was recovered (−)-2-ethylhexanoic acid (1·25 g., 83%), b. p. 223°, α^{15}_{5893} −1·80° (*l* 0·5), whence the acid had undergone 40% racemisation.

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278. *Indicator Measurements with Amines in Anisole and Chlorobenzene Solution.*

By R. P. BELL and J. W. BAYLES.

The basic strengths of 21 amines have been compared in anisole and chlorobenzene solutions by measuring their equilibria with the indicators 2 : 6-dinitrophenol and bromophenol-blue. The data are best interpreted quantitatively by assuming that the binary complexes of base and indicator are not associated further in solution, and do not dissociate into ions. The indicator constants in chlorobenzene differ very little from those in anisole. The values obtained provide a more rational account of the effect of alkyl substitution on basic strength than do dissociation constants in water, and it is concluded that the anomalies in the latter are largely due to hydrogen-bonding with the solvent. The indicator constants for amines in anisole bear a close relationship to their catalytic constants in the decomposition of nitramide in the same solvent.

IF dissociation constants in water are used as a measure of the basic strengths of amines there are many apparent anomalies in the relations between structure and strength (cf., *e.g.*, the numerous data given by Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469). In particular, it appears that the dissociation constants of primary, secondary, and tertiary amines are not directly comparable, and this effect has been attributed to hydrogen-bonding between water molecules and either the amine molecules (Moore and Winmill, *J.*, 1912, **101**, 1635) or their cations (Trotman-Dickenson, *J.*, 1949, 1293; Evans and Hammann, *Trans. Faraday Soc.*, 1951, **47**, 34). It is therefore desirable to obtain data for the basic strengths of amines in non-hydroxylic solvents, and this is most readily done by means of indicator measurements. It is well known that there are often difficulties in the quantitative interpretation of indicator measurements in non-aqueous solvents (cf., *e.g.*, LaMer and Downes, *J. Amer. Chem. Soc.*, 1931, **53**, 888; Baggesgaard-Rasmussen and Reimers, *Dansk Tidsskr. Farm.*, 1933, **7**, 225; Griffiths, *J.*, 1938, 818), and our aim in the present investigation has been to obtain approximate comparable values for a large number of amines rather than to make an exact quantitative study of any one system. The solvents used were chlorobenzene and anisole, since these are devoid of any acidic properties and have been used previously in kinetic work on acid–base catalysis.

EXPERIMENTAL

Chlorobenzene and anisole were distilled, dried over phosphoric oxide, and redistilled through a column. The indicators used were 2 : 6-dinitrophenol and bromophenol-blue: the former was recrystallized from alcohol (m. p. 63·0°), and both were dried *in vacuo* over phosphoric oxide. Most of the amines were dried over potassium hydroxide for several days and then distilled. Their b. p.s were within 1° of the accepted values. *p*-Toluidine was dissolved in ligroin and shaken with activated alumina. It was then recrystallized twice and dried over phosphoric oxide *in vacuo* (m. p. 45°). Quinoline was precipitated as dichromate, which was decomposed by potassium hydroxide, and the amine separated by steam distillation, drying, and distilling *in vacuo*. *iso*Quinoline was partially frozen, distilled, and then fractionally frozen three times (m. p. 23—23·5°). All the amines were colourless, and gave colourless solutions in chlorobenzene and anisole.

The glass-ware and optical cells used for solutions were baked for at least 2 hours at 150—170° before use, and left in a vacuum-desiccator over pellets of potassium hydroxide. If these

precautions were not taken some of the bromophenol-blue was liable to be adsorbed as a yellow film on the glass surfaces. This adsorption was particularly strong with soda-glass, and all cells and other vessels used were of Pyrex or Hysil glass. The absorption of the solutions was measured with a Hilger Spekker absorptiometer, 1-cm. cells and the mercury 4047 Å line being used. In making a measurement, the cell was warmed slightly above 25°, and the reading taken when it had cooled to 25° after a few minutes in the instrument.

Dry solutions of both indicators are colourless, but on adding amine solution a yellow colour is produced and reaches a constant absorption when a large excess of base is added. Typical figures are given in Table 1. The negligible absorption found at 5780 Å shows that the change

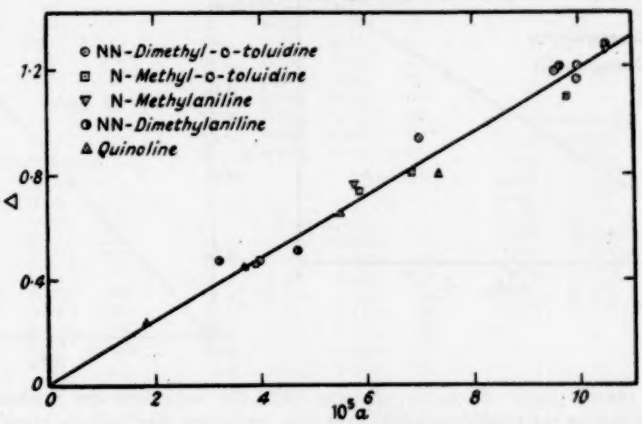
TABLE 1. *Addition of* NN-*dimethyl-o-toluidine to bromophenol-blue in chlorobenzene.*

(Δ = change produced in drum reading by addition of amine; indicator concentration = $0{\cdot}952 \times 10^{-4}$ mole/litre.)

[Amine]	$3{\cdot}65 \times 10^{-5}$	$1{\cdot}82 \times 10^{-4}$	$9{\cdot}12 \times 10^{-4}$	$1{\cdot}82 \times 10^{-3}$	$9{\cdot}12 \times 10^{-3}$	$1{\cdot}0 \times 10^{-1}$	$2{\cdot}0 \times 10^{-1}$
Δ(4047 Å) ...	0·23	0·64	0·08	1·14	1·18	1·22	1·22
Δ(5780 Å) ...	$0{\cdot}00_2$	$0{\cdot}00_6$	$0{\cdot}00_5$	$0{\cdot}00_7$	$0{\cdot}00_8$	0·02	0·01

yellow ⟶ blue (normally used in aqueous solution) is not involved, and the same is true for all the aromatic and heterocyclic amines studied. With strong aliphatic amines, on the other

FIG. 1. *Bromophenol-blue in chlorobenzene.*



hand, bromophenol-blue gives a red or purple colour (cf. Davis, Schuhmann, and Lovelace, *J. Res. Nat. Bur. Stand.*, 1948, **41**, 27) and was therefore not used for studying these amines. Similarly, 2 : 6-dinitrophenol with some aromatic bases gives a brown colour which differs from the usual yellow colour of the basic form. It is thought that this phenomenon is due to complex formation of the same type which occurs between nitro-compounds and a variety of aromatic hydrocarbons, and 2 : 6-dinitrophenol was therefore only used with aliphatic amines.

With the above reservations the absorption at 4047 Å of the basic form of each indicator was proportional to the indicator concentration and approximately independent of the nature of the amine which had been added in excess. This is illustrated in Figs. 1—3, which give plots of the Spekker reading Δ (proportional to the extinction coefficient of the solution) against the indicator concentration a. It may therefore be assumed that the change observed represents a true acid–base reaction, and that any association phenomena which may occur have little effect on the validity of Beer's law. Similar results are obtained in other solvents, and Table 2 gives the molar extinction coefficients of the basic form of bromophenol-blue in various solvents. The variations are no greater than would be expected from the changes of medium involved.

TABLE 2. *Molar extinction coefficients* (ε) *of the basic form of bromophenol-blue.*

Solvent	$10^{-3}\varepsilon$	Solvent	$10^{-3}\varepsilon$	Solvent	$10^{-3}\varepsilon$
Chlorobenzene	11·1	Carbon tetrachloride	14·2	Dioxan	11·4
Anisole	12·2	Chloroform	12·5	Ethyl acetate	14·2

Calculation of Equilibrium Constants.— The measurements of colour lead directly to the proportion of indicator in the basic form, but the further treatment of the results depends upon what assumption is made about the state of the reaction products, in particular whether the ions formed are free or are associated together in some way. We have calculated equilibrium constants on the assumption of association to form ion-pairs; *i.e.*, if B is the base and IH the indicator, the indicator constants are defined by

$$[BH^+,I^-]/[B][IH] = K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

This choice is supported by accurate work on the reaction between tribenzylamine and picric acid in benzene solution (Davis and McDonald, *J. Res. Nat. Bur. Stand.*, 1949, **42**, 595) which agrees well with equation (1). The concentration of free ions in such solutions is negligible (Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 3614), and measurements of dielectric constant indicate that the further association of the ion-pairs is small at the concentrations used here (Maryott, *J. Res. Nat. Bur. Stand.*, 1948, **41**, 1). With some systems the values of K have a tendency to increase with increase in colour, as would be expected if further association

FIG. 2. *Bromophenol-blue in anisole.*

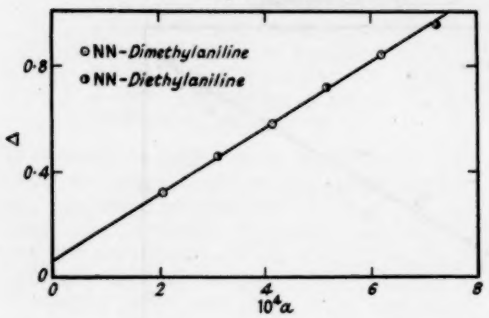
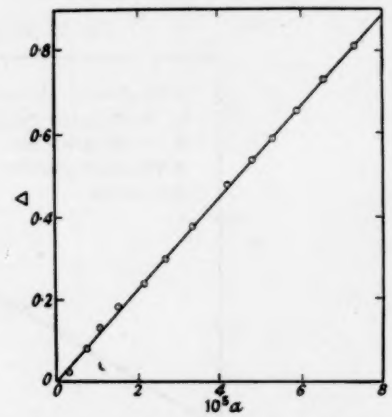


FIG. 3. *Excess of* n-*butylamine added to* 2 : 6-*dinitrophenol in chlorobenzene.*



of ion-pairs is taking place. However, in most cases the variations are random, and other methods of calculating the equilibrium constant (*e.g.*, assuming free ions, or binary association of ion pairs) give large systematic variations. If a is the total indicator concentration, b the concentration of base added, and r the ratio [coloured form of indicator]/[colourless form of indicator], then equation (1) becomes

$$r(1 + r)/[b(1 + r) - ar] = K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

This equation was used in calculating all the constants given in the following tables, r being derived directly from the Spekker reading and the absorption of the basic form of the indicator as shown in Figs. 1—3.

Tables of Results.—In the following tables all concentrations are expressed in moles per litre of solution, and the error attached to the mean values of the constants represents the probable error calculated from the usual statistical expressions.

TABLE 3. 2 : 6-*Dinitrophenol in chlorobenzene.*

10^4b	10^4a	r	$10^{-3}K$	10^4b	10^4a	r	$10^{-3}K$	10^4b	10^4a	r	$10^{-3}K$
	n-*Butylamine.*				*Di*-n-*butylamine.*				*Tri*-n-*butylamine.*		
0·974	1·06	0·122	14	0·293	1·06	0·213	200	0·335	1·06	0·393	990
2·82	1·06	0·422	17	0·677	1·06	0·515	160	0·658	1·06	0·937	650
3·70	1·06	0·581	18	0·971	1·06	0·852	180	0·978	1·06	1·77	590
5·35	1·06	0·852	19	1·57	1·06	1·60	170	1·27	1·06	2·81	580
8·32	1·06	1·17	15	2·44	1·06	2·71	160	1·83	1·06	5·03	530
		Mean	16 ± 1			Mean	690 ± 140			Mean	170 ± 10

TABLE 4. *Bromophenol-blue in chlorobenzene.*

10^4b	10^4a	r	K
	Aniline.		
27·1	0·800	0·0236	8·7
56·4	0·996	0·0331	5·9
56·4	0·996	0·0490	8·7
113	0·996	0·134	12
82·2	1·15	0·0763	9·3
137	1·15	0·226	17
138	1·15	0·216	16
45·1	1·20	0·0292	6·5
116	1·44	0·210	18
96	1·73	0·057	16
24·1	2·78	0·0186	7·7
12·1	5·76	0·0153	13
5·50	6·42	0·0056	10
		Mean	11 ± 3
	o-Toluidine.		
403	0·599	0·667	17
58	0·996	0·059	10
173	0·996	0·250	15
289	0·996	0·567	20
532	0·996	1·46	27
115	1·60	0·211	18
		Mean	18 ± 4
	N-Ethyl-o-toluidine.		
3·86	0·50	0·120	310
15·4	0·50	0·49	320
3·26	1·00	0·086	230
7·72	1·00	0·170	230
9·65	1·00	0·27	280
11·6	1·00	0·312	270
15·4	1·00	0·43	280
19·3	1·00	0·54	290
3·86	2·00	0·080	220
11·6	2·00	0·25	220
		Mean	270 ± 20
	NN-Dimethyl-p-toluidine.		
1·32	0·50	0·33	2800
2·64	0·50	0·69	2800
0·33	1·00	0·089	3600
0·66	1·00	0·180	3500
1·32	1·00	0·36	3400
2·64	1·00	0·69	3100
0·33	2·00	0·075	4000
0·66	2·00	0·150	3700
1·32	2·00	0·30	3500
		Mean	3400 ± 300
	Quinoline.		
0·734	0·50	0·40	6700
1·00	0·50	0·73	9300
0·220	1·00	0·110	9200
0·430	1·00	0·235	9700
1·12	1·00	0·60	8100
2·15	1·00	1·03	6300
5·91	1·00	2·50	4800
1·00	2·00	0·35	7200
		Mean	7500 ± 400

10^4b	10^4a	r	K
	N-Methylaniline.		
5·54	0·288	0·0246	44
11·1	0·288	0·056	50
1·38	1·44	0·0099	73
2·77	1·44	0·0163	60
4·80	1·44	0·0315	66
		Mean	59 ± 7
	NN-Dimethylaniline.		
0·820	0·321	0·051	640
1·23	0·321	0·081	680
10·2	0·321	0·567	560
0·614	1·61	0·041	750
1·54	1·61	0·085	600
3·08	1·61	0·165	580
		Mean	630 ± 40
	N-Methyl-o-toluidine.		
107	0·390	0·725	70
67·0	0·585	0·350	52
84·4	0·683	0·480	57
6·70	0·975	0·050	75
18·1	0·975	0·102	57
26·8	0·975	0·151	57
67·0	0·975	0·469	70
121	0·975	0·781	65
		Mean	63 ± 5
	p-Toluidine.		
14·0	0·332	0·031	22
14·0	0·527	0·065	46
5·0	1·05	0·028	57
8·0	1·05	0·032	40
20·0	1·05	0·125	63
30·0	1·05	0·264	88
40·0	1·05	0·508	130
8·0	2·10	0·054	69
14·0	2·10	0·134	97
		Mean	65 ± 20
	N-Ethyl-p-toluidine.		
1·57	0·50	0·23	1600
3·14	0·50	0·56	1900
0·785	1·00	0·089	1300
1·57	1·00	0·23	1600
3·14	1·00	0·56	2000
0·785	2·00	0·104	1700
1·57	2·00	0·25	2100
3·14	2·00	0·57	2400
		Mean	1800 ± 100
	isoQuinoline.		
0·290	0·50	0·22	11000
0·580	0·50	0·57	14000
0·870	0·50	0·93	15000
0·290	1·00	0·23	18000
0·290	1·00	0·21	18000
0·580	1·00	0·44	16000
0·870	1·00	0·65	14000
0·580	2·00	0·27	17000
		Mean	15000 ± 500

10^4b	10^4a	r	K
	N-Ethylaniline.		
6·36	0·50	0·190	300
12·7	0·50	0·326	260
3·18	1·00	0·089	290
6·36	1·00	0·173	280
12·7	1·00	0·452	360
1·59	2·00	0·043	280
3·18	2·00	0·089	300
6·36	2·00	0·202	340
		Mean	300 ± 20
	NN-Diethylaniline.		
0·323	0·50	0·386	21000
0·646	0·50	0·906	22000
0·323	1·00	0·312	37000
0·646	1·00	0·671	27000
0·646	2·00	0·394	49000
		Mean	29000 ± 3000
	NN-Dimethyl-o-toluidine.		
1·99	0·398	0·57	3100
4·07	0·398	1·23	3100
9·04	0·398	3·71	4300
3·98	0·697	1·10	3000
9·04	0·697	2·92	3400
0·994	0·995	0·27	3400
1·99	0·995	0·51	3100
3·98	0·995	1·01	2900
5·97	0·995	1·56	2900
9·04	0·995	2·46	3000
		Mean	3200 ± 300
	N-Methyl-p-toluidine.		
3·72	0·50	0·160	450
1·86	1·00	0·058	320
3·72	1·00	0·140	390
7·44	1·00	0·33	460
1·86	2·00	0·094	550
1·86	3·66	0·087	560
		Mean	460 ± 50
	Pyridine.		
1·34	0·50	0·36	3000
1·69	0·50	0·53	3500
3·38	0·50	1·03	3300
0·669	1·00	0·160	3000
0·845	1·00	0·244	3800
1·34	1·00	0·33	3000
1·69	1·00	0·45	3300
0·334	2·00	0·070	3500
0·669	2·00	0·133	3100
0·845	2·00	0·196	3800
		Mean	3300 ± 200

TABLE 5. *Bromophenol-blue in anisole.*

10^4b	10^4a	r	K
	Aniline.		
170	0·50	0·21	12
340	0·50	0·38	11
85	1·00	0·072	9
116	1·00	0·126	11
170	1·00	0·075	10
340	1·00	0·39	11
85	2·00	0·072	9
170	2·00	0·24	14
		Mean	11 ± 1
	N-*Methylaniline.*		
54·6	0·50	0·23	43
137	0·50	0·73	53
27·3	1·00	0·143	53
54·6	1·00	0·35	64
137	1·00	0·70	51
13·7	2·00	0·076	56
27·3	2·00	0·150	56
54·6	2·00	0·34	63
		Mean	55 ± 4
	NN-*Dimethylaniline.*		
2·45	0·50	0·169	710
4·90	0·50	0·35	740
9·80	0·50	0·64	670
1·23	1·00	0·098	860
2·45	1·00	0·165	710
2·45	1·00	0·174	760
4·90	1·00	0·34	730
1·23	2·00	0·089	840
4·09	2·00	0·30	680
		Mean	740 ± 40
	N-*Ethylaniline.*		
10·3	0·50	0·28	270
20·6	0·50	0·53	260
41·2	0·50	1·03	250
5·15	1·00	0·145	290
10·3	1·00	0·298	290
20·6	1·00	0·56	280
5·15	2·00	0·121	250
10·3	2·00	0·24	240
		Mean	270 ± 10
	o-*Chloroaniline.*		
1290	0·50	0·34	2·6
1310	0·50	0·27	2·1
647	1·00	0·074	1·1
655	1·00	0·107	1·6
1290	1·00	0·176	1·4
1310	1·00	0·145	1·1
2590	1·00	0·369	1·4
647	2·00	0·043	0·7
655	2·00	0·049	0·8
1290	2·00	0·082	0·6
		Mean	1·3 ± 0·2
	m-*Chloroaniline.*		
4050	0·50	0·87	2·1
1010	1·00	0·093	0·9
1350	1·00	0·176	0·9
2030	1·00	0·207	1·0
1010	2·00	0·070	0·6
2030	2·00	0·143	0·7
		Mean	0·9 ± 0·2

10^4b	10^4a	r	K
	o-*Toluidine.*		
157	0·50	0·102	6·5
314	0·50	0·24	7·6
157	1·00	0·117	7·5
314	1·00	0·29	9·2
629	1·00	0·86	14
79	2·00	0·072	9·2
157	2·00	0·170	10·9
		Mean	9·3 ± 1·6
	N-*Methyl*-o-*toluidine.*		
61·8	0·50	0·26	41
123·6	0·50	0·61	49
30·9	1·00	0·145	47
61·8	1·00	0·35	58
123·6	1·00	0·68	55
30·9	2·00	0·150	49
61·8	2·00	0·301	49
		Mean	48 ± 4
	NN-*Dimethyl*-o-*toluidine.*		
1·46	0·50	0·47	3600
2·92	0·50	0·92	3400
0·73	1·00	0·24	4500
0·73	1·00	0·175	4100
1·46	1·00	0·40	3400
0·37	2·00	0·098	5300
		Mean	4100 ± 500
	N-*Ethyl*-o-*toluidine.*		
6·60	0·50	0·26	400
13·2	0·50	0·59	450
26·4	0·50	1·41	490
3·30	1·00	0·13	420
6·60	1·00	0·23	350
13·2	1·00	0·51	400
1·65	2·00	0·043	280
3·30	2·00	0·072	230
6·60	2·00	0·15	230
		Mean	360 ± 70
	p-*Toluidine.*		
38·2	0·50	0·19	50
76·4	0·50	0·38	50
19·1	1·00	0·103	54
38·2	1·00	0·21	56
76·4	1·00	0·47	62
19·1	2·00	0·117	62
38·2	2·00	0·22	60
		Mean	56 ± 3
	N-*Methyl*-p-*toluidine.*		
4·94	1·00	0·136	280
9·88	1·00	0·30	310
19·7	1·00	0·68	350
4·94	2·00	0·150	320
9·88	2·00	0·32	340
9·88	2·00	0·30	330
19·7	2·00	0·64	310
		Mean	320 ± 15
	NN *Diethylaniline.*		
0·516	0·50	0·77	13000
1·03	0·50	1·76	20000
0·258	1·00	0·24	38000
0·516	1·00	0·51	28000
		Mean	25000 ± 3000

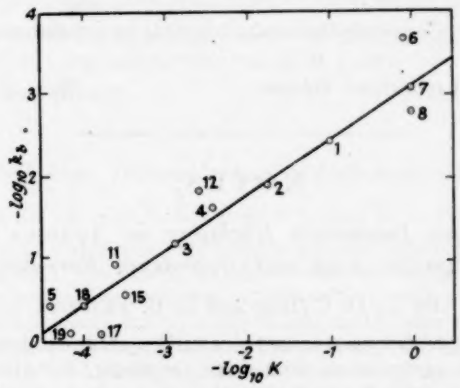
10^4b	10^4a	r	K
	p-*Chloroaniline.*		
2400	0·50	0·140	0·6
600	1·00	0·062	1·0
1200	1·00	0·136	1·1
2400	1·00	0·313	1·3
300	2·00	0·023	0·8
600	2·00	0·057	0·9
		Mean	0·9 ± 0·2
	NN-*Dimethyl*-p-*toluidine.*		
0·523	0·50	0·130	2800
1·05	0·50	0·25	2600
0·262	1·00	0·063	3100
0·523	1·00	0·126	3100
1·05	1·00	0·23	2700
0·262	2·00	0·055	3500
0·523	2·00	0·101	3100
		Mean	3000 ± 200
	N-*Ethyl*-p-*toluidine.*		
1·42	0·50	0·17	1300
2·84	0·50	0·32	1200
0·71	1·00	0·081	1300
1·42	1·00	0·16	1300
2·84	1·00	0·29	1100
0·71	2·00	0·053	900
1·42	2·00	0·120	1000
		Mean	1100 ± 100
	Pyridine.		
0·70	0·50	0·32	5500
1·40	0·50	0·56	4600
0·35	1·00	0·140	6200
0·35	1·00	0·140	6200
0·70	1·00	0·26	5300
0·70	1·00	0·28	5800
1·40	1·00	0·51	4800
1·40	1·00	0·54	5100
0·35	2·00	0·103	6300
0·70	2·00	0·44	5500
		Mean	5600 ± 400
	Quinoline.		
0·427	0·50	0·26	7800
0·853	0·50	0·53	7800
0·213	1·00	0·117	11000
0·427	1·00	0·22	8800
0·853	1·00	0·46	8500
0·213	2·00	0·081	13000
0·427	2·00	0·160	11000
		Mean	9700 ± 1000
	iso*Quinoline.*		
0·366	0·50	0·30	12000
0·732	0·50	0·64	12000
0·183	1·00	0·122	17000
0·366	1·00	0·22	12000
0·732	1·00	0·49	12000
0·183	2·00	0·074	17000
0·366	2·00	0·145	13000
		Mean	14000 ± 1500

TABLE 6. *Summary of results with bromophenol-blue in chlorobenzene and anisole.*

pK_b values in water from Hall and Sprinkle (*J. Amer. Chem. Soc.*, 1932, **54**, 3469); k_b = catalytic constant in the decomposition of nitramide (Bell and Trotman-Dickenson, *J.*, 1949, 1288).

	Base	$-\log_{10} K$ PhCl	$-\log_{10} K$ Ph·OMe	pK_b (H_2O)	$-\log_{10} k_b$ (Ph·OMe)
1.	Aniline	−1·0	−1·0	9·42	2·46
2.	*N*-Methylaniline	−1·8	−1·74	9·15	1·92
3.	*NN*-Dimethylaniline	−2·80	−2·87	8·94	1·19
4.	*N*-Ethylaniline	−2·48	−2·43	8·89	1·64
5.	*NN*-Diethylaniline	−4·5	−4·4	7·44	0·44
6.	*o*-Chloroaniline	—	−0·1	11·4	3·70
7.	*m*-Chloroaniline	—	0·0	10·48	3·11
8.	*p*-Chloroaniline	—	0·0	10·00	2·83
9.	*o*-Toluidine	−1·26	−1·0	9·61	—
10.	*N*-Methyl-*o*-toluidine	−1·80	−1·68	9·41	—
11.	*NN*-Dimethyl-*o*-toluidine	−3·51	−3·61	8·14	0·94
12.	*N*-Ethyl-*o*-toluidine	−2·43	−2·6	9·07	1·83
13.	*p*-Toluidine	−1·8	−1·75	8·93	—
14.	*N*-Methyl-*p*-toluidine	−2·66	−2·51	8·67	—
15.	*NN*-Dimethyl-*p*-toluidine	−3·53	−3·48	8·50	0·58
16.	*N*-Ethyl-*p*-toluidine	−2·43	−2·6	9·07	1·83
17.	Pyridine	−3·52	−3·75	8·63	0·09
18.	Quinoline	−4·0	−3·99	9·00	0·44
19.	*iso*Quinoline	−4·2	−4·15	8·76	−0·11

FIG. 4.



DISCUSSION

The indicator constants obtained are not of high accuracy, but are adequate for a semi-quantitative discussion of the effect of substitution. Table 6 shows that the values of K in chlorobenzene and anisole lie very close together in spite of considerable differences in chemical nature and dielectric constant of the solvents. This is good evidence that neither solvent is playing any specific part in determining the position of equilibrium, and the data are therefore more suitable than basic strengths in aqueous solution for judging the effects of substituents. This appears most clearly in the results for the three butylamines in chlorobenzene (Table 3). The three indicator constants are 1600, 17 000, and 69 000 for the primary, secondary, and tertiary amine, respectively, showing the expected progressive effect of introducing the butyl groups. In aqueous solution, on the other hand, the values of pK_b are 3·39, 2·69, and 4·07: the unexpected rise from the secondary to the tertiary amine occurs also with other aliphatic amines in water, and is no doubt due to hydrogen-bonding between the water and the amine cations (cf. Trotman-Dickenson, *loc. cit.*).

The indicator constants for the aromatic amines (Table 6) follow the expected trends, which do not differ qualitatively from those found in aqueous solution. Successive substitution of methyl groups in the amino-group increases the basic strength, the second one producing a larger change than the first. The effect of ethyl is considerably greater than that of methyl. A methyl group in the ring *o*- or *p*- to the amino-group also increases the basic strength, though the effect is smaller than that of *N*-substitution. Here again some of the results in water are anomalous, since *o*-toluidine appears to be a weaker base than aniline, and *p*-toluidine stronger than *N*-methylaniline.

It is of interest to compare the indicator constants of the aromatic and heterocyclic amines in anisole with their catalytic constants in the decomposition of nitramide in the same solvent, measured by Bell and Trotman-Dickenson (*J.*, 1949, 1288). The latter are recorded as $-\log_{10} k_b$ in Table 6, and Fig. 4 shows a plot of $\log_{10} k_b$ against $\log_{10} K$. There is an approximately linear relation over more than four powers of ten in K, and there are no signs of the systematic deviations found if dissociation constants in water are used as a measure of basic strength, when separate linear relationships are found for the classes of primary, secondary, tertiary, and heterocyclic amines. Similar behaviour has been observed in the base-catalysed decomposition of nitramide in *iso*amyl alcohol (Brönsted, Delbanco, and Tovborg-Jensen, *Z. physikal. Chem.*, 1934, **169**, *A*, 361), where the observed catalytic constants are related simply to basic strengths measured in the same solvent, but not to basic strengths in water. It is likely that the same situation will arise whenever the range of acid–base systems used as catalysts involves substitution on the atom bearing the proton, since under these conditions the effect of substituents upon acid–base strength in polar solvents will often be complicated by solvation effects.

Our thanks are due to Monsanto Chemicals, Limited, for a maintenance grant to one of us (J. W. B.).

PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, December* 31*st*, 1951.]

NOTES.

279. *Hydrogen–Deuterium Exchange in Aqueous Solutions of Glycollic Acid and of Sodium Formate.*

By L. D. C. BOK and L. B. PETTERS.

THE rate of exchange of hydrogen attached to a carbon atom, rendered measurable by the presence of a carboxyl group as an immediate neighbour, is further influenced by the nature of other atoms or radicals attached to the same carbon atom. Thus measurement of the rate of this exchange in a series of saturated fatty acids gives information on the relative influence of various substituents.

By carrying out a number of exchange experiments with aqueous solutions of glycollic acid at 210°, 200°, and 190°, averaging the calculated first-order velocity constants, and extrapolating the plot of $\log_{10} k$ against $1/T$, 330 hours has been obtained as the calculated approximate time of half-change for the forward (protium-rich substance + deuterium-rich solvent) exchange of the $C_{(\alpha)}$-hydrogen, and 470 hours for the reverse reaction at 160°.

The result for the forward exchange may be compared with the values obtained under the same conditions for other acids—800 hours for sodium formate (Bok and Cohen, *J. South African Chem. Inst.*, in the press), 40 hours for potassium acetate (Bok and Geib, *Z. phys. Chem.*, 1939, *A*, **183**, 353), and 1·4 hours for glycine (Bok and Mitchell, *J. South African Chem. Inst.*, in the press). The electromeric effect of the hydroxyl oxygen would result in the α-carbon atom being more electronegative; on the other hand the inductive effect of the positive ammonium ion results in a depletion of the electrons from the α-carbon atom. Thus one would expect the order glycollic acid < acetic acid < glycine for a reaction involving a proton transfer from the α-carbon atom.

An approximate activation energy calculated for the hydrogen exchange in glycollic acid is 30 kcals.

Sodium formate partly converted into formic acid by addition of deuterium chloride exchanged the $C_{(a)}$-hydrogen at about the same rate as the formate ion. The exchange was more rapid when excess of deuterium chloride was present.

Experimental.—Weighed quantities of pure glycollic acid (about 0·1 g.) and deuterium oxide (about 0·5 g.) were heated in sealed Pyrex-glass tubes (15 cm. × 0·75 internal diam.) in an oil-bath whose temperature was thermostatically controlled to within 0·1°. After the required time the solvent was distilled off under vacuum, and the substance was redissolved in water at room temp. The solvent was again distilled off, the substance dried under high vacuum, and then burned in a stream of dry oxygen, and the isotopic content of the water formed determined by the method described by Harteck (*Z. Electrochem.*, 1938, **44**, 3).

For study of the reverse exchange, a forward-exchange experiment was carried out using four times the quantities stated above, and considerable exchange allowed to take place. Part of the material was used for combustion and the measurement of isotopic content, and the remainder for reverse-exchange experiments, about 0·1 g. of deuterated substance and 0·5 ml. of water being used.

A similar procedure was used with sodium formate. Deuterium chloride was prepared by distilling deuterium oxide on to barium chloride–phosphorus pentachloride, and distilling off the deuterium chloride formed, together with excess of deuterium oxide. Deuterium chloride solutions, about 5N, were obtained, the normality being determined by titration of about 0·1 ml. of the solution with standard sodium hydroxide. The deuterium chloride solution could be diluted with deuterium oxide to the required normality. With sodium formate, the acid was neutralised before distillation of the solvent, with standard sodium hydroxide solution.

We are indebted to the South African Council for Scientific and Industrial Research for Grants for equipment and expenses to one of us (L. D. C. B.).

UNIVERSITY OF NATAL, DURBAN. [*Received, October 30th*, 1951.]

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280. *Methylene Derivatives of* D-*Galactose and* D-*Glucose.*

By L. HOUGH, J. K. N. JONES, and M. S. MAGSON.

THE condensation of formaldehyde with sugars was first recorded by Schulz and Tollens (*Annalen*, 1896, **289**, 20; *Ber.*, 1899, **32**, 2585) who, by treatment of grape sugar with formaldehyde in the presence of concentrated hydrochloric acid, obtained a crystalline product, containing a free reducing group; analysis indicated a monomethylene glucose. Later work by De Bruyn and Van Eckenstein (*Rec. Trav. chim.*, 1903, **22**, 159) led to the isolation of syrupy bismethylene derivatives of glucose and galactose from a melt of the sugars with paraformaldehyde in the presence of an acid catalyst. Further investigation by Schmidt, Distelmaier, and Heiss ("F.I.A.T. Review of German Science, Preparative Organic Chemistry," Part II, p. 90) has provided evidence for the presence of a free hydroxyl group on $C_{(6)}$ of bismethylene glucose. This conclusion follows from the formation of 6-methyl glucose from bismethylene glucose.

Following De Bruyn and Van Eckenstein's procedure (*loc. cit.*) we attempted to condense D-glucose and also D-galactose with formaldehyde by melting the sugar and paraformaldehyde with a little acid catalyst; very little of the desired products was obtained. In an attempt to obtain a homogeneous reaction D-glucose was heated with paraformaldehyde in glacial acetic acid with concentrated sulphuric acid as catalyst, and a crystalline acetyl bismethylene derivative was obtained. The syrupy bismethylene glucose, obtained from the acetyl derivative, yielded, on methylation, a crystalline methyl bismethylene derivative which, on hydrolysis, gave 6-methyl D-glucose. It is established, therefore, that bismethylene glucose has a free primary alcohol grouping on $C_{(6)}$, and it follows that the acetyl and methyl derivatives must be 6-acetyl and 6-methyl bismethylene D-glucose.

A similar series of derivatives has been prepared from D-galactose. In this case, how-

ever, the acetyl bismethylene derivative was not obtained crystalline, but deacetylation followed by methylation with Purdie's reagents gave a crystalline methyl bismethylene D-galactose. Hydrolysis of this gave crystalline 6-methyl D-galactose, thus providing conclusive evidence that, in bismethylene galactose, formaldehyde is not engaged in acetal formation with the hydroxyl group on $C_{(6)}$.

Whilst the structures of the methylene derivatives of the hexose sugars await solution, those of many of the polyhydric alcohols are known. Thus, for example, Ness, Hann, and Hudson (*J. Amer. Chem. Soc.*, 1944, **66**, 665, 670) have proved that 1 : 3-2 : 4-5 : 6-tris-methylene sorbitol is obtained when formaldehyde reacts with sorbitol.

The bismethylene derivatives of galactose and glucose which we have prepared are non-reducing to Fehling's solution and show no mutarotation. It is clear that the formaldehyde residues may be attached in acetal formation with hydroxyl groups, other than those on $C_{(6)}$, on adjacent carbon atoms, or other carbon atoms, but that one residue must involve the $C_{(1)}$-glycosidic hydroxyl group. Thus the methylene residues on glucose or galactose could be represented as 1 : 2-3 : 4-, 1 : 3-2 : 4-, or even 1 : 4-2 : 3-, assuming that the sugars exist in the pyranose form, which is by no means certain. Furthermore, isomerism may arise through the α- and β-glycosidic forms.

Experimental.—Carbon and hydrogen determinations are by Drs. Weiler and Strauss, Oxford, and methoxyl by Mr. W. M. Eno, Bristol. M. p.s are uncorrected. Optical rotations were determined in a 10-cm. tube, aqueous solutions being used.

6-Acetyl bismethylene D-*glucose.* A solution of D-glucose (50 g.) in water (20 c.c.) was mixed with glacial acetic acid (200 c.c.); paraformaldehyde (55 g.) was then added, followed by cautious addition, with shaking, of sulphuric acid (*d* 1·84; 25 c.c.). The mixture was heated on the steam-bath for 1 hour, the clear yellow solution was then cooled, water (200 c.c.) was added, and the liquor was extracted thrice with chloroform (200-c.c., 100-c.c., and 100-c.c. portions). The combined chloroform extracts were repeatedly washed with water until the washings were neutral. The chloroform solution was then dried ($CaCl_2$), filtered, and evaporated under reduced pressure to a syrup (37·6 g.) which partially crystallised. The crystalline material was isolated on a tile and recrystallised from methylated spirits, giving *6-acetyl bismethylene* D-*glucose* (9 g.), m. p. 104°, $[\alpha]_D$ +46·5° (*c*, 0·67) (Found: C, 48·8; H, 5·6; Ac, 16·7. $C_{10}H_{14}O_7$ requires C, 48·75; H, 5·7; Ac, 17·5%).

6-Methyl bismethylene D-*glucose.* 6-Acetyl bismethylene D-glucose (4·7 g.) was dissolved in methanol (10 c.c.), and a solution of sodium methoxide (0·5 g.) in methanol (10 c.c.) added. The methanol was evaporated under reduced pressure and the syrupy deacetylated product methylated by heating it under reflux with methyl iodide (20 c.c.) and silver oxide (20 g.; added in four portions during 6 hours). The reaction mixture was extracted with chloroform, filtered, and the clear solution evaporated under reduced pressure to yield crystalline *6-methyl bismethylene* D-*glucose* (2·2 g.) which was recrystallised from absolute alcohol. It had m. p. 46°, $[\alpha]_D$ +45° (*c*, 1·14) (Found: C, 49·3; H, 6·2; OMe, 14·5. $C_9H_{14}O_6$ requires C, 49·5; H, 6·4; OMe, 14·2%).

6-Methyl D-*glucose.* A solution of 6-methyl bismethylene D-glucose (0·5 g.) in 2N-hydrochloric acid (2 c.c.) was heated at 100° for 3 hours. The cooled solution was neutralised by treatment with Amberlite resin IR-4B, and unchanged material extracted with chloroform. Evaporation of the neutral aqueous solution in a vacuum-desiccator afforded crystalline 6-methyl D-glucose (0·1 g.) which was recrystallised from ethyl alcohol and then had m. p. 140° (mixed m. p. with an authentic specimen 137—138°), $[\alpha]_D$ +89° (initial value) ⟶ +61° ± 3° (equilibrium; *c*, 0·29). An *X*-ray powder photograph of the crystals was identical with that of 6-methyl D-glucose. 6-Methyl glucose is readily separable from the 2-, 3-, or 4-methyl derivatives on the paper chromatogram by using the butanol–pyridine–water solvent (Hough, Jones, and Wadman, *J.*, 1950, 1702). The chromatogram was run for 30 hours to achieve good separation of the sugars, and on development with *p*-anisidine hydrochloride it was observed that 3- and 4-methyl glucose gave spots of higher R_F value, which were yellower than that of 6-methyl glucose. 2-Methyl glucose also moved at a faster rate than 6-methyl glucose, but gave a redder spot. The rates of movement of the methyl derivatives relative to rhamnose of assumed R_F 0·30 were 2- (0·27), 3- (0·29), 4- (0·27) and 6- (0·25), respectively. The corresponding figures in the butanol–ethanol–water solvent (40 : 11 : 19) were 0·28, 0·29, 0·25, and 0·24. After separation in this solvent, 6-methyl glucose gave a redder derivative with the spray reagent than did the 2-methyl glucose. The 6-methyl bismethylene D-glucose may be hydrolysed at 100°

by agitating it with a suspension of Amberlite resin IR 120 (Wadman, unpublished results; cf. Glen, Myers, and Grant, *J.*, 1951, 2568) in water containing a weight of resin equivalent to a 0·25N-solution for 3 hours. To isolate the sugar it is necessary only to filter and evaporate the solution; the product is free from coloured decomposition products which are usually present when mineral acids are employed for the hydrolysis.

6-*Acetyl bismethylene* D-*galactose*. The condensation of formaldehyde with D-galactose (50 g.) in glacial acetic acid with sulphuric acid catalyst followed the technique already described for glucose and gave syrupy 6-methyl bismethylene D-glactose (14 g.). Distillation of the product under reduced pressure gave a syrup which failed to crystallise even after several months.

6-*Methyl bismethylene* D-*galactose*. The above syrup (14 g.) was converted into the methyl derivative by dissolving it in a little methanol and proceeding as described for the corresponding glucose derivative. A crystalline solid (10 g.) was obtained which, on recrystallisation from light petroleum (b. p. 60—80°) gave 6-*methyl bismethylene* D-*galactose* (5·5 g.), m. p. 82—82·5°, $[\alpha]_D$ −55·5° (*c*, 1·37) (Found: C, 49·6; H, 6·3; OMe, 14·4. $C_9H_{14}O_6$ requires C, 49·5; H, 6·4; OMe, 14·2%).

6-*Methyl* D-*galactose*. Hydrolysis of the bismethylene compound (0·5 g.), as described for the glucose compound, gave a crystalline product which after recrystallisation from *n*-butanol had m. p. 119·5—120·5° (mixed m. p. 120—121°), $[\alpha]_D$ +117·5° (initial value ⟶ constant value). An *X*-ray powder photograph of the crystals was identical with that of an authentic secimen of 6-methyl D-glactose. 6-Methyl galactose is distinguished from the 2-, 3-, or 4-methyl derivatives by paper chromatography, the butanol–pyridine–water (*idem*, *ibid.*) mixture being used as mobile phase. 3- and 4-Methyl galactose gave lower R_F values (0·21 and 0·20, respectively) and were yellower than the synthetic material which moved at the same rate as 6-methyl galactose (R_F 0·22). 2-Methyl galactose (R_F 0·25) gave a redder spot than 6-methyl galactose (cf. the colour differentiation in the glucose derivatives). The rates of movement of the methyl glucoses in the butanol–ethanol–water solvent were 2- (0·24), 3- (0·20), 4- (0·19), and 6- (0·20), respectively.

We thank Dr. T. Malkin for *X*-ray analyses and one of us (M. S. M.) acknowledges receipt of an F.E.T.S. grant from the Ministry of Education.

THE UNIVERSITY, BRISTOL 8. [*Received, December 18th*, 1951.]

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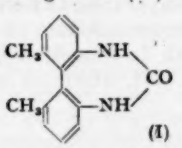
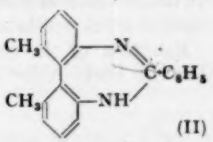
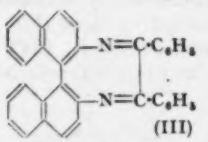
281. *The Stereochemistry of 2 : 2′-Bridged Derivatives of Diphenyl.*

By F. BELL.

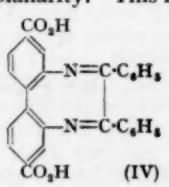
KUHN AND GOLDFINGER (*Annalen*, 1929, **470**, 183) obtained (III) in an optically active condition by the interaction of (+)-2 : 2′-diamino-1 : 1′-dinaphthyl with benzil, and Sako (*Mem. Coll. Eng. Kyushu*, 1932, **6**, 283) obtained compounds (I) and (II) in active forms starting from (−)-2 : 2′-diamino-6 : 6′-dimethyldiphenyl. It was recognised that

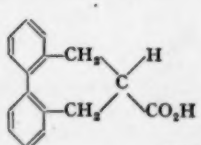

(I)


(II)


(III)

the ring system based on the 2 : 2′-positions of the diphenyl must exist in a non-planar form but the presence of obstacle groups in the 6 : 6′-positions was regarded as essential to preserve the non-planarity. This is now found to be unnecessary.


(IV)


(V)

Compound (IV), obtained by the interaction of 2 : 2′-diaminodiphenyl-4 : 4′-dicarboxylic acid and benzil, is readily resolved by crystallisation of the brucine salt to give

optically stable enantiomorphs. This result suggests that the compound (V) might be resolvable, but attempted resolution has so far failed.

Experimental.—2 : 2′-Diaminodiphenyl-4 : 4′-dicarboxylic acid (Jakubowski and Niementowski, *Ber.*, 1909, **42**, 650) was heated in a bath at 260° with the calculated quantity of benzil. The product was dissolved in sodium carbonate solution and reprecipitated with acetic acid. It was very sparingly soluble in acetone, chloroform, and *o*-dichlorobenzene but more soluble in boiling alcohol, acetic acid, cellosolve, and formamide. **6 : 7-*Diphenyl*-5 : 8-*diaza*-1 : 2-3 : 4-*dibenzo*cyclo*octatetraene*-2′ : 2″-*dicarboxylic acid*** (IV) crystallised from these solvents on addition of water in pale yellow prisms, m. p. 348° (Found : C, 75·0; H, 4·1; N, 6·5. $C_{28}H_{18}O_4N_2$ requires C, 75·3; H, 4·0; N, 6·3%). On addition of (IV) (1·4 g.) to brucine (2·8 g.) in hot ethanol (50 c.c.) there was obtained a clear solution which almost immediately began to deposit rosettes of needles. The crop ($[\alpha]_D$ −540°; c = 1, in chloroform) was extracted with alcohol until constant rotatory power was obtained ($[\alpha]_D$ −566°). On decomposition with hydrochloric acid this gave the free acid, $[\alpha]_D$ −740° (c = 1, in N/2-sodium hydroxide) raised by crystallisation from aqueous alcohol to $[\alpha]_D$ −955°. The mother liquor from the brucine salt was concentrated, a small crystalline crop removed, and the residual liquor poured into dilute hydrochloric acid. The product had $[\alpha]_D$ +925° (c = 0·91, in N/2-sodium hydroxide).

The compound formed from 2 : 2′-diaminodiphenyl and benzil had m. p. 238° in agreement with Tauber (*Ber.*, 1892, **25**, 3287). It had negligible solubility in cold acetone and cold ethanol, low solubility in cold acetone, and moderate solubility in cold benzene and cold pyridine. Attempted resolution by adsorption from benzene solution on powdered cellulose or lactose was unsuccessful. The compound could be readily recrystallised from amyl alcohol or limonene.

1 : 2-3 : 4-Diben*zocyclo*hepta-1 : 3-diene-6-carboxylic acid (V) (Kenner, *J.*, 1913, **103**, 621) yielded non-crystalline brucine, morphine, quinidine, strychnine, and cinchonine salts. The quinine and cinchonidine salts could be readily recrystallised from ethanol, but the acid recovered from all crops was optically inactive.

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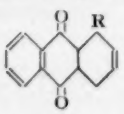
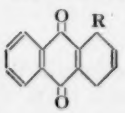
282. 1-o-*Methoxyphenylanthraquinone.*

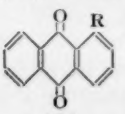
By E. A. BRAUDE and J. S. FAWCETT.

1-*o*-METHOXYPHENYLANTHRAQUINONE has been synthesised in the following manner. Reaction of *o*-methoxyphenylmagnesium bromide with crotonaldehyde gave *o*-methoxyphenylpropenylcarbinol (I), which undergoes oxotropic rearrangement to *o*-methoxystyrylmethylcarbinol (II) on treatment with dilute mineral acid and dehydration to 1-*o*-methoxyphenylbuta-1 : 3-diene (III) on distillation from potassium hydrogen sulphate (cf. Braude, Jones, and Stern, *J.*, 1947, 1087). Reaction of the diene with 1 : 4-naphthaquinone in ethanol at room temperature afforded the Diels–Alder adduct (IV), which, on treatment in hot alkaline solution with a current of oxygen, was oxidised to a mixture of the dihydroanthraquinone (V) and the anthraquinone (VI).

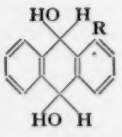
o-MeO·C_6H_4·CH(OH)·CH:CHMe (I) *o*-MeO·C_6H_4·CH:CH·CHMe·OH (II) *o*-MeO·C_6H_4·CH:CH·CH:CH_2 (III)


(IV)


(V)


(VI)

(VII)


(VIII)

R = *o*-C_6H_4·OMe

On treatment with hot sodium dithionite (hydrosulphite) solution, 1-*o*-methoxyphenylanthraquinone is not reduced to the corresponding anthraquinol, but to a derivative which contains one less oxygen atom and is formulated as 1-*o*-methoxyphenyl-9-anthrone (VII).* The anthrone is readily oxidised back to the anthraquinone in alkaline solution. Treatment of 1-*o*-methoxyphenylanthraquinone with lithium aluminium hydride at 0° gave a tetrahydro-derivative, formulated as 9 : 10-dihydro-1-*o*-methoxyphenylanthraquinol (VIII) on the basis of its ultra-violet light absorption properties. Under similar conditions, anthraquinone itself is stated to give anthraquinol (Nystrom and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3738) whereas anthracene does not react (Sampey and Cox, *J. Amer. Chem. Soc.*, 1949, **71**, 1507; Goodman, *J.*, 1951, 2209). On the other hand, the action of lithium aluminium hydride on 1 : 2-anthraquinone has been shown to give 1 : 2-dihydroanthraquinol (Booth, Boyland, and Turner, *J.*, 1950, 1188).

Experimental.—o-*Methoxyphenylpropenylcarbinol.* Freshly distilled crotonaldehyde (38 g.) in ether (100 ml.) was added to *o*-methoxyphenylmagnesium bromide (from magnesium, 13 g.; ethyl bromide, 0·5 g.; and *o*-bromoanisole, 100 g.) in ether (300 ml.) during 1 hour at 0° in an atmosphere of nitrogen. Stirring was continued for 2 hours, and excess of saturated ammonium chloride solution added at 0°. The ethereal layer was separated and dried (Na_2SO_4). Distillation from a trace of anhydrous potassium carbonate afforded o-*methoxyphenylpropenylcarbinol* (58 g., 67%) as a colourless liquid, b. p. 88°/0·05 mm., n_D^{23} 1·5431 (Found: C, 73·8; H, 7·9. $C_{11}H_{14}O_2$ requires C, 74·15; H, 7·9%). Light absorption in ethanol: $\lambda_{max.}$ 2230, 2730, and 2780 Å, ε = 8900, 2500, and 2300, respectively.

o-*Methoxystyrylmethylcarbinol.* The above carbinol (6 g.) was dissolved in a 0·01M-solution of hydrochloric acid in 60% aqueous acetone (100 ml.), and the solution kept for 24 hours at room temperature. On dilution with water, o-*methoxystyrylmethylcarbinol* (5 g.) separated as a viscous oil, which was distilled and had b. p. 100°/0·03 mm., n_D^{23} 1·5691 (Found: C, 74·3; H, 8·1. $C_{11}H_{14}O_2$ requires C, 74·15; H, 7·9%). Light absorption in ethanol: $\lambda_{max.}$ 2510 and 2990 Å, $\lambda_{infl.}$ 2560 Å, ε = 15 800, 5200, and 15 300, respectively. The p-*nitrobenzoate* crystallised from benzene–light petroleum (b. p. 80—100°) in colourless clusters of needles, m. p. 109° (Found: C, 66·6; H, 5·4; N, 4·4. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·2; N, 4·3%). Light absorption in ethanol: $\lambda_{max.}$ 2560 and 2950 Å, $\lambda_{infl.}$ 2640 Å, ε = 36 000, 8500, and 29 800, respectively.

1-o-*Methoxyphenylbutadiene.* *o*-Methoxyphenylpropenylcarbinol (50 g.) was heated with anhydrous potassium hydrogen sulphate (5 g.) to 60° for 10 minutes and then rapidly distilled to give 1-o-*methoxyphenylbutadiene* (27 g., 60%), b. p. 68°/0·05 mm., n_D^{23} 1·6169 (Found: C, 82·9; H, 7·7. $C_{11}H_{12}O$ requires C, 82·5; H, 7·6%). Light absorption in ethanol: $\lambda_{max.}$ 2260, 2730, 2770, 3100, and 3160, $\lambda_{infl.}$ 2810 Å, ε = 14 400, 24 500, 24 000, 12 800, 12 800, and 23 200, respectively.

1-o-*Methoxyphenylanthraquinone.* A solution of the above diene (1 g.) and naphthaquinone (1 g.) in ethanol (6 ml.) was kept at room temperature for 48 hours. Filtration gave 1 : 4 : 13 : 14-*tetrahydro*-1-*o*-*methoxyphenylanthraquinone* (1·3 g.), which crystallised from ethyl acetate in colourless prisms, m. p. 154—155° (Found: C, 79·2; H, 5·8. $C_{21}H_{18}O_3$ requires C, 79·2; H, 5·7%).

The tetrahydroanthraquinone (5 g.) was dissolved in ethanol (100 ml.) containing potassium hydroxide (1 g.) and oxygen was passed through the hot solution for 15 minutes. After cooling, the product (4·8 g.) was filtered off and separated into two fractions by treatment with hot methanol (300 ml.). From the methanol-soluble fraction, 1-o-*methoxyphenylanthraquinone* (3 g.) was obtained, which crystallised from methanol in yellow prisms and rods, m. p. 160° (Found: C, 80·1; H, 4·75. $C_{21}H_{14}O_3$ requires C, 80·3; H, 4·5%). Light absorption in chloroform: $\lambda_{max.}$ 2440, 2495, 2670, and 3350 Å, ε = 22 000, 24 000, 19 000, and 3300, respectively. The methanol-insoluble fraction gave 1 : 4-*dihydro*-1-o-*methoxyphenylanthraquinone* (1 g.), which crystallised from xylene in yellow needles, m. p. 208° (Found: C, 79·8; H, 5·3. $C_{21}H_{16}O_3$ requires C, 79·8;* H, 5·1%). Light absorption in chloroform: $\lambda_{max.}$ 2590 and 4130 Å, $\lambda_{infl.}$ 2640 Å, ε = 19 000, 1500, and 17 500, respectively.

Reduction of 1-o-*methoxyphenylanthraquinone.* (*a*) The quinone (3 g.) was suspended in a solution of sodium dithionite (4 g.) in 5% sodium hydroxide solution (50 ml.), and the mixture refluxed for 1 hour in an atmosphere of nitrogen. The product, formulated as 1-o-*methoxyphenyl*-9-*anthrone*, crystallised from methanol in colourless rods, m. p. 158° (Found: C, 83·8; H, 5·6. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·3%). On treatment with 1% alcoholic potassium hydroxide solution the anthrone was readily re-oxidised to the quinone.

* The alternative 10-anthrone structure is not excluded.

(*b*) Lithium aluminium hydride (0·2 g.) in ether (20 ml.) was slowly added to a solution of the quinone (1 g.) in benzene (50 ml.) at 0°, and the whole stirred at room temperature for 30 minutes; excess of 2N-sulphuric acid was added, and the ether–benzene extract evaporated, to give 9 : 10-*dihydro*-1-o-*methoxyphenylanthraquinol* (0·8 g.), which crystallised from methanol in colourless rectangular prisms, m. p. 195—196° (Found : C, 79·1; H, 6·0. $C_{21}H_{16}O_2$ requires C, 79·25; H, 5·65%). Light absorption in ethanol : $\lambda_{max.}$ 2800 Å, $\varepsilon = 3200$.

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283. *The Separation of α-Acetamido-acids by Partition Chromatography on Kieselguhr.*

By G. HOWARD SMITH.

THE technique recently devised by Stein and Moore (*Cold Spr. Harb. Sym. Quant. Biol.*, 1949, **14**, 179; *J. Biol. Chem.*, 1951, **192**, 663) for the chromatographic separation of amino-acids on ion-exchange resins is much superior to the original partition method described by Martin and Synge (*Biochem. J.*, 1941, **35**, 1358) and Gordon, Martin, and Synge (*ibid.*, 1943, **37**, 79; 1944, **38**, 65) for the quantitative microanalysis of amino-acid mixtures. The latter technique has, however, certain advantages for preparative work in that the bands are made visible on the column by the use of an indicator held in the stationary phase and the α-acetamido-acids so separated can, if necessary, be estimated easily, quickly, and without their destruction, by titration with baryta solution.

One drawback to the partition method is the extreme degree of unreproducibility in the preparation of the silica gel used to support the stationary (aqueous) phase. Even those batches of silica which were satisfactory for the other faster-moving acetamido-acids still adsorbed acetyltryptophan to a greater or less extent, rendering separation in good yield of small quantities of this substance difficult or impossible (G. H. Smith, Ph.D. Thesis, University of London, 1950). At Dr. A. J. P. Martin's suggestion, columns were therefore prepared from kieselguhr. In addition to other advantages over precipitated silica, kieselguhr is almost non-adsorptive (Martin, *Biochem. Soc. Sym.*, 1949, **3**, 4), and it was found to give very satisfactory columns, which would carry a high load of acetyltryptophan.

The performance of the columns was highly reproducible. As an example, 9·9 mg. of acetyltryptophan ($R = 0·5$) was just separated from 7·4 mg. of acetylphenylalanine ($R = 0·9$) and well separated from 7·0 mg. of acetylvaline ($R = 0·2$) on a column (0·9 cm. × 10·2 cm.) containing 4·0 g. of kieselguhr. In several runs, estimated recoveries of acetylphenylalanine of 98—102% and of acetyltryptophan of 98—104% were obtained. The recovery of acetylvaline was only about 90% but the reason for this was not determined. By collection and separate titration of 1-ml. fractions of the eluate, it was shown that the zones were only slightly tailed at this column-loading. The degree of separation was, of course, greater for smaller amounts of the acids. The immediate aim of this work, however, was not so much to obtain a complete separation for analytical purposes, as to obtain a convenient and rapid method of isolating 5—10 mg. of tryptophan from protein hydrolysates for isotope analysis. It is suggested that the use of kieselguhr partition columns containing indicator in the stationary phase could be of wide applicability in the separation of acids and bases on a micro-preparative scale.

Experimental.—Hyflo "Supercel" (Johns–Manville Co. Ltd.) (about 150 g.) was added to water (1 l.) without stirring, and allowed to settle, and the yellow supernatant liquid and some floating material were decanted off. The wet kieselguhr was made into a column 5·8 cm. in diameter which was washed with 2N-nitric acid (500 ml.) to remove interfering metals and then with water until the effluent was neutral (methyl-orange). The column was sucked as dry as possible and extruded. The kieselguhr was then successively dried at 110°, roasted in a muffle furnace for 1½ hours to remove residual organic matter, and sieved (90 mesh).

For use in columns, the washed kieselguhr was first thoroughly mixed with 0·015% methyl-orange solution (0·5 ml. per 1 g. of kieselguhr) and dried at 110°. It was then mixed with the amount of 0·1N-sulphuric acid previously determined to give the most satisfactory colour of

the indicator (usually about 0·6 ml. acid to 1 g. of kieselguhr), and then redried. The acidified solid was not kept in the oven for more than 3—4 hours or at room temperature for more than a day before use, as it tended to become more alkaline. Water was added to the kieselguhr (0·7 ml. per 1 g.), and the mixture suspended in *n*-butanol–chloroform (1% by volume; water-saturated) in the usual way. Although the kieselguhr would hold appreciably more than its own weight of water without appearing wet, columns containing the above amount were the easiest to pack in 1% butanol in chloroform solution and were therefore generally used. The columns were packed with the aid of a perforated metal disc on the end of a long wire (Martin, *loc. cit.*) and then run in the usual way without regulation of the rate of flow of the developing solvent. The separated acetamido-acids were titrated with 0·01N-barium hydroxide (bromothymol-blue) (Gordon *et al.*, 1943, *loc. cit.*).

As kieselguhr is less adsorbent than silica gel, the methyl-orange was held less firmly in the stationary phase if the columns were prepared as for silica; the drying of the indicator on to the kieselguhr appeared largely to fix it, however. Nevertheless, a small amount of indicator was sometimes displaced by the substances being separated, particularly from the top of the column, but this effect was overcome by placing small pads of acid-treated kieselguhr containing water but no indicator at the top and bottom of the column. Liddell and Rydon's indicator (*Biochem. J.*, 1944, **38**, 68) might perhaps have been held more firmly, being less soluble in organic solvents, but methyl-orange was used owing to its greater sensitivity. The indicator was, of course, rapidly eluted by chloroform containing 20% *n*-butanol.

The author thanks Dr. A. J. P. Martin, F.R.S., for his advice and Sir Paul Fildes, O.B.E., F.R.S., and Dr. H. N. Rydon for their interest. This work was carried out during the tenure of a Leverhulme Research Scholarship.

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284. 2 : 4 : 5-*Trichlorophenetole.*

By F. E. Smith.

In another investigation, it became necessary to prepare pure 2 : 4 : 5-trichlorophenetole. The only references to this are in D.R.-P. 411,052 (Agfa, 1925) and U.S.P. 2,072,797 (Gen. Electric Co., 1937). Both processes describe preparations from 1 : 2 : 4 : 5-tetrachlorobenzene, alcohol, and sodium hydroxide, which are heated under pressure, in the first case alone, and in the second case in the presence of cuprous chloride. Only Agfa describe the product, which is stated to crystallise from alcohol with m. p. 95°. This is unexpectedly high, since substituted phenetoles in general melt at lower temperatures than the corresponding anisoles and parent phenols.

2 : 4 : 5-Trichlorophenetole, prepared by treatment of the pure phenol with ethyl sulphate in alkaline solution, followed by recrystallisation from ethanol, then methanol, had m. p. 40·4°, unchanged by boiling dilute sodium hydroxide or by recrystallisation from toluene, so, as it seemed certain that the product was that required, the Agfa process was repeated.

1 : 2 : 4 : 5-Tetrachlorobenzene (7·3 g.), sodium hydroxide pellets (2·5 g.), and anhydrous industrial alcohol (50 ml.) were heated at 170—180° for 7 hours in a sealed tube. When cool, the mixture was transferred to a flask with the aid of water (100 ml.) and steam-distilled, giving: (*a*) an alcoholic fraction which on evaporation to dryness gave 0·2 g., m. p. 37°; (*b*) the main ether fraction which was separated and dried, giving 3·3 g. of oil + crystals; and (*c*) the phenol fraction, distilled after acidification with sulphuric acid, which was filtered off and dried, giving 3·5 g., m. p. 54—55°, mixed m. p. with pure 2 : 4 : 5-trichlorophenol 59—62·5°. The material from (*b*) was recrystallised three times from methanol until short colourless needles, m. p. 40·3°, were obtained. As these were identical in appearance and m. p. with the material prepared by alkylation, and as the mixed m. p. was 40·3°, it is evident that the m. p. 95° recorded for 2 : 4 : 5-trichlorophenol is incorrect and that the true m. p. is 40·4°.

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285. 4 : 6-*Dichloro*-2-*dimethylaminopyrimidine.*

By W. R. Boon.

King and King (*J.*, 1947, 726) have described the isolation of two substances from the reaction of 2 : 4 : 6-trichloropyrimidine with dimethylamine. To the substance, m. p. 113°, they assigned the structure 2 : 4-dichloro-6-dimethylaminopyrimidine, and a second substance of m. p. 102—103° was believed to be 4 : 6-dichloro-2-dimethylaminopyrimidine. On repetition of this work no difficulty was encountered in obtaining the higher-melting isomer pure, but only solids of indefinite m. p. could be obtained when using the conditions prescribed by King and King for the isolation of the low-melting isomer. Fractional crystallisation of such a mixture first from aqueous methanol and then from light petroleum showed it to consist of 2 : 4-dichloro-6-dimethylamino- and 4 : 6-dichloro-2-dimethylamino-pyrimidine, m. p. 54°. The latter substance has also been prepared by the reaction of 2-dimethylamino-4 : 6-dihydroxypyrimidine with phosphorus oxychloride. Reaction of this substance with ammonia, methylamine, and dimethylamine gave respectively 4-amino-6-chloro-2-dimethylamino-, 4-chloro-2-dimethylamino-6-methylamino- and 4-chloro-2 : 6-bisdimethylamino-pyrimidine, the first two compounds being identical with the corresponding compounds prepared by reaction of dimethylamine with 4-amino-2 : 6-dichloropyrimidine (Büttner, *Ber.*, 1903, **36**, 2227) and 2 : 4-dichloro-6-methylaminopyrimidine (Winklemann, *J. pr. Chem.*, 1927, **115**, 292).

Experimental.—2-*Dimethylamino*-4 : 6-*dihydroxypyrimidine.* Dimethylguanidine sulphate (91 g.) was stirred for 30 minutes with a boiling solution of sodium methoxide, from sodium (15 g.) and methanol (300 c.c.). Ethyl malonate (116 g.) was then added cautiously and the whole was stirred under reflux for 6 hours. After cooling, water (450 c.c.) was added, the solution acidified with acetic acid, and the *pyrimidine* collected (85 g.). It did not melt below 350° and for analysis was crystallised from water (Found: C, 41·6; H, 6·4; N, 24·6. $C_6H_9O_2N,3H_2O$ requires C, 41·6; H, 6·4; N, 24·2%).

4 : 6-*Dichloro*-2-*dimethylaminopyrimidine.* (*a*) 2-Dimethylamino-4 : 6-dihydroxypyrimidine (15·5 g.; dried at 120°) and phosphorus oxychloride (60 c.c.) were heated under reflux for 35 minutes, cooled, and poured with stirring into cold 2N-sodium hydroxide (1 l.); after 15 minutes the *dichloro*-compound was collected; purified first by steam-distillation and then by crystallisation from light petroleum, it (16 g.) had m. p. 54° (Found: C, 37·6; H, 3·8; N, 21·8; Cl, 36·4. $C_6H_7N_3Cl_2$ requires C, 37·5; H, 3·7; N, 21·9; Cl, 36·9%). (*b*) This substance was also isolated by fractional crystallisation, alternately from light petroleum and aqueous methanol, of the residue remaining after removal of the bulk of the 2 : 4-dichloro-6-dimethylaminopyrimidine from the reaction product of trichloropyrimidine and dimethylamine (King and King, *loc. cit.*).

4-*Amino*-6-*chloro*-2-*dimethylaminopyrimidine.* 2-Dimethylamino-4 : 6-dichloropyrimidine (3·8 g.) and 10% ethanolic ammonia (10 c.c.) were heated at 110—120° for 18 hours. After the mixture had cooled, water was added, the crude product collected, and unchanged starting material removed by steam-distillation. The *aminopyrimidine*, crystallised first from benzene–light petroleum and then from aqueous ethanol, had m. p. 151° (Found: C, 41·5; H, 5·5; N, 32·8; Cl, 19·7. $C_6H_9N_4Cl$ requires C, 41·7; H, 5·2; N, 32·5; Cl, 20·6%). The same product (identified by m. p. and mixed m. p.) was obtained by reaction of 4-amino-2 : 6-dichloropyrimidine (3·3 g.) with dimethylamine (3 g. in 15 c.c. of ethanol) at 80° for 10 hours.

4-*Chloro*-2-*dimethylamino*-6-*methylaminopyrimidine*, m. p. 78° (from aqueous ethanol), b. p. 122—125°/1 mm. (Found: C, 45·4; H, 6·1; N, 30·6; Cl, 19·0. $C_7H_{11}N_4Cl$ requires C, 45·1; H, 5·9; N, 30·0; Cl, 19·0%), was obtained similarly from 4 : 6-dichloro-2-dimethylaminopyrimidine and alcoholic methylamine or 2 : 4-dichloro-6-methylaminopyrimidine and alcoholic dimethylamine.

4-*Chloro*-2 : 6-*bisdimethylaminopyrimidine*, m. p. 52·5° after sublimation at 56°/0·1 mm. (Found: C, 47·4; H, 6·1; N, 27·1; Cl, 17·5. $C_8H_{13}N_4Cl$ requires C, 47·8; H, 6·5; N, 27·9; Cl, 17·7%), was similarly obtained from 4 : 6-dichloro-2-dimethylaminopyrimidine and alcoholic dimethylamine.

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Atoms and Radicals in Aqueous Media.

THE TILDEN LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY AT BURLINGTON HOUSE ON FEBRUARY 15TH, 1951, AND AT THE UNIVERSITY COLLEGE, HULL, ON MARCH 1ST, 1951.

By F. S. DAINTON.

THE presence in the H_2O molecule of the $(2sa_1)^2$ and $(2xb_1)^2$ non-bonding electrons of the oxygen atom combined with the non-linear arrangement of the two polar O–H linkages has many important consequences in chemistry. One of these consequences, namely, the very high capacity of liquid water to solvate ionic and polar solutes, is probably the greatest single factor determining the special features of the chemistry of atoms and free radicals in aqueous media. In this Lecture my aim will be, not to catalogue all the extensive work in this field, but rather to draw attention to certain recently developed threads of reasoning which are generally applicable, and to the slightly different patterns into which these threads may be woven to account for the observed phenomena. Such a selection of topics has, of course, been to some extent arbitrary and personal, and has certainly led to many important omissions. Some of the material is new, and I am greatly indebted to my colleagues, especially Messrs. Collinson, James, and Smith, for their help and for permission to use their data.

Methods of Detection.

1. *General.*—The majority of the radicals which have been prepared in aqueous systems are of very short life and therefore can only be detected by the stable molecules to which they give rise by chemical reaction. These reactions include all those diverse processes which are characteristic of all odd-electron species. Thus we find hydrogen atoms combining and perhydroxy-radicals undergoing disproportionation:

$$2H \longrightarrow H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$2HO_2 \longrightarrow H_2O_2 + O_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Inter-radical reactions of this kind are especially favoured in water because the dissociation energy of the reaction $H_2O \longrightarrow H + OH$ (~120 kcal. in the gas phase) is so large that nearly all reactions which involve the detachment of either a hydrogen atom or a hydroxyl radical from the water are endothermic *e.g.*,[1]

$$\cdot NH_{2(g)} + H_2O_{(g)} \longrightarrow NH_{3(g)} + \cdot OH_{(g)} - 16 \text{ kcal.} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The most important exceptions to this generalisation are the thermoneutral exchange reactions (*e.g.*, $HO + H_2O \longrightarrow H_2O + OH$) discussed later. The rarity of radical–water reactions means that water is in many ways an ideal medium for studying the reactivity of radicals with other solutes. Such radical–molecule reactions are of the kind expected. For example, Weiss [2] has shown that OH radicals abstract H atoms from dissolved benzene (~ 0·01M-solution) with resultant formation of diphenyl and phenol. In addition to such *adiabatic* reactions, many radicals may act as oxidising or reducing agents by virtue of their respective capacities to accept and donate electrons in *single-electron transfer* processes. The driving force of such reactions is discussed in greater detail later, but in passing we may note that a very important part of this driving force is the free energy of hydration of the ion produced. For example, in the reduction of cations such as Fe^{3+} by hydrogen atoms

$$H + Fe^{3+}_{aq.} \longrightarrow H^+_{aq.} + Fe^{2+}_{aq.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

the solvation energy of the H^+ ion which is formed is extremely large.[3] Because the amount of product formed in such simple reactions is limited by the stoicheiometry, these reactions can only be used for detection and estimation of small concentrations of radicals, provided a sensitive method of estimating the product is available. Usually, colorimetric methods are employed.[4] Another method of achieving the desired sensitivity is to magnify the effect of individual radicals by employing them as centres for the initiation of chain reactions. The type of chain reaction which is most productive of information concerning the initiating radical is the polymerisation of water-soluble vinyl compounds.

[1] Based on $D_{NH_2 \ldots H(g)} = 104$ kcal., see Szwarc, *Proc. Roy. Soc.*, 1949, *A*, **198**, 267.
[2] Weiss and Stein, *Nature*, 1947, **161**, 650.
[3] Baughan, *J.*, 1940, 1335.
[4] *E.g.*, Miller, *J. Chem. Physics*, 1950, **18**, 79.

2. *The Polymerisation Method.*—Electrophilic substituents in ethylene confer two properties on the molecule : those of enhanced solubility in polar solvents and of increased ease of addition polymerisation by the free-radical mechanism. When radicals (X) are generated in aqueous solutions of a monomer (m_1) such as acrylonitrile, methyl acrylate, or acrylic acid, the following reactions may ensue which result in the formation of an insoluble polymer

Initiation	$X + m_1 \xrightarrow{k_i} m_1^*$	(5)
Propagation	$m_1 + m_j^* \xrightarrow{k_p} m_{j+1}^*$	(6)
Mutual termination	$m_j^* + m_k^* \xrightarrow{k_t} P_{j+k}$ or $P_j + P_k$	(7)
Radical termination	$m_j^* + X \xrightarrow{k'_t} P_j$	(8)

In this scheme m_j^* denotes the growing polymer radical containing j segments of monomer, and P_j denotes " dead " polymer incapable of further growth. Solvent transfer can be omitted from this scheme when water is the solvent, because of the pronounced endothermic character of reactions of this type.

The kinetic chain length of the polymerisation chain, *i.e.*, the number of monomer molecules polymerised per radical X used in initiation, is very large and implies an unusually high ratio,

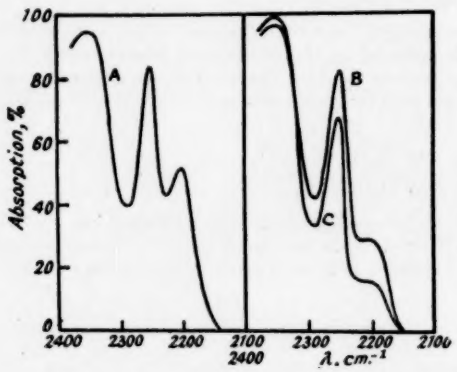

FIG. 1. *The infra-red absorption spectra in the range 4·16—4·78 μ of samples of polyacrylonitrile prepared by the action of 250 kv X-rays on acrylonitrile : A in solution in D_2O, B in solution in H_2O, C pure monomer. Dose rate, 680 r/min. The peak at ~2200 cm.⁻¹ is the 4·58 μ band due to C–D stretching vibration.*

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k_p/k_t or k_p/k'_t. This is result is very convenient since the kinetic chain length is the " magnification factor " to be used in estimating the concentration of the radicals. Even with very low rates of generation of radicals such as are obtained with low dose rates of ionising radiation, such polymerisations may readily be followed by dilatometric,[5] gravimetric,[6] or turbidimetric [7] methods. The initiation reaction consists of the opening of the double bond of the monomer, thereby fixing the radical X to the polymer in the form of a C–X end-group. An advantage of the polymerisation method is that the nature of such end-groups can readily be determined and the chemical nature of the radical X can therefore be discovered. Chemical methods of end-group analysis can be used, but these are generally less reliable than infra-red spectroscopic analysis of the polymer. Absorption bands present in the polymer produced by X-radical initiation which are either absent from polymers produced from pure monomers or diminish in intensity with increasing chain length of the polymer can be safely ascribed to the end-groups. In this way it has been possible to show that OH radicals are produced by the photo-dissociation of hydrogen peroxide in aqueous solution or when X- and γ-rays are absorbed by water.[6b] The great power of the infra-red method is evident when proof is required of the presence of hydrogen atoms derived from the solvent water. When D_2O is the solvent the polymer should contain a terminal C–D link which has a characteristic frequency at ~4·58 μ (2200 cm.⁻¹). Fig. 1 shows quite unmistakably that whereas polyacrylonitrile prepared by X-irradiation of the pure monomer does not show this absorption band, the polymer formed by irradiation of solutions of acrylonitrile in deuterium oxide does possess this band. The infra-red measurements thus

[5] Collinson and Dainton, to be published.
[6] (*a*) Dainton, *Nature*, 1947, **160**, 268; (*b*) *J. Phys. Coll. Chem.*, 1948, **52**, 490.
[7] Smith, unpublished data.

provide incontrovertible evidence of the existence of H atoms and OH radicals in water which is absorbing ionising radiation.

One of the features of the polymerisation method is that it may be used to distinguish between a system in which the radicals are uniformly distributed and one in which they are localised. As an example of the type of argument which may be employed we may consider a stationary number (x) of initiating radicals (X) uniformly distributed throughout a reaction volume V, such that the concentration (x/V) is sufficiently low to ensure that the predominant mode of chain termination is by mutual interaction of a pair of growing polymer chains [reaction (7)]. This is substantially, although not exactly, the state of affairs when H atoms or OH radicals are produced photochemically under conditions of low light extinction and low light intensity.[8] The rate of polymerisation is then given by

$$\frac{-\mathrm{d}[\mathrm{m}_1]}{\mathrm{d}t} = \left(\frac{\phi_1 I_{\mathrm{abs.}}}{k_t}\right)^{\frac{1}{2}} k_p[\mathrm{m}_1] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

in which ϕ_1 is the quantum yield of formation of H or OH in the act of light absorption and $I_{\mathrm{abs.}}$ is the absorbed light intensity. An alternative situation may also be envisaged in which the same total number of radicals (x) are non-uniformly arranged in the same total volume V. We may imagine them confined to n small, widely separated, elements of volume v, such that $nv \ll V$. The concentration in each volume element ($= x/nv$) may now be so large that radical termination [reaction (8)] predominates over mutual termination, *i.e.*, $k_t[\mathrm{m}_j^{\bullet}]_v^2 < k_t'[\mathrm{m}_j^{\bullet}]_v(x/nv)$. In this case the overall rate of polymerisation will be given by

$$\frac{-\mathrm{d}[\mathrm{m}_1]}{\mathrm{d}t} = \frac{nv}{V} \cdot \frac{k_i k_p}{k_t'}[\mathrm{m}_1]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

An example of this type of behaviour when the initiation is both by H atoms and by OH radicals will be given in the next section.

In using photosensitisers of high extinction for the initiation of reaction chains, care must be taken to avoid such high rates of generation of initiating centres that radical termination becomes excessive and the polymerisation method misleading. For example, Mr. James has found that, in certain cases in which it was known from the changes undergone by the photosensitiser that hydrogen atoms were being formed, no visible polymerisation occurred. Further analysis of the problem showed that the monomer was either hydrogenated or merely converted into water-soluble short-chain polymers. That this was due to excessive radical termination was strikingly shown by reducing the sensitiser concentration a thousand-fold, whereupon insoluble polymer was freely formed, throughout the reaction vessel.[8]

Certain other precautions must be observed in using polymerisation diagnostically. The most important is to deaerate the solutions thoroughly. Oxygen may act as a powerful chain terminator by direct addition to the growing polymer chain, and is also capable of inhibiting action by destroying certain initiating radicals. For example, hydrogen atoms are removed by the reaction

$$\mathrm{H} + \mathrm{O}_2 \longrightarrow \mathrm{HO}_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

and the resulting species can act as a chain terminator,[7] *i.e.*,

$$\mathrm{HO}_2 + \mathrm{m}_j^{\bullet} \longrightarrow \mathrm{P}_j\mathrm{O}_2\mathrm{H} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

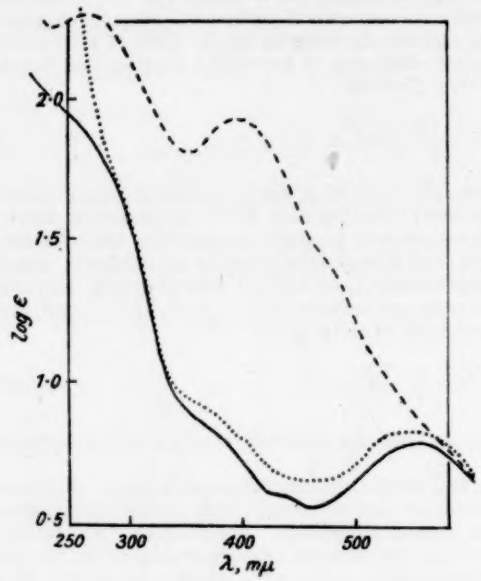
The effect of traces of dissolved oxygen is so marked that complete eradication of induction periods due to this cause is only achieved by the most stringent conditions of deaeration. Fortunately, however, the steady rate of the polymerisation reaction is independent of the length of any induction period by which it may have been preceded.

The sensitivity of the polymerisation technique increases with increasing concentration of monomer, and the value of a particular monomer for this purpose is thus enhanced the more soluble it is in water. Acrylonitrile is particularly satisfactory from this point of view, but in one respect, namely, the marked tendency to form complexes with cations, it is somewhat unsuitable. For instance, the bivalent vanadium ion, V^{2+}, gives lavender-coloured solutions, and its electron-transfer spectrum has a long-wave absorption edge at 3500 Å (see Fig. 2). When acrylontrile is added to solutions of vanadous sulphate, VSO_4, the lavender colour is immediately

[8] Dainton and James, *J. Chim. physique*, in the press.

replaced by a brown colour similar to that of the vanadocyanide ion $[V(CN)_6]^{4-}$ and an entirely new absorption region between 3500 and 5400 Å is observed (Fig. 2). The spectrum of vanadic sulphate solutions, $V_2(SO_4)_3$, is unaffected by addition of acrylonitrile (Fig. 3). The spectro-

FIG. 2. *The effect of methyl acrylate* (MA) *and acrylonitrile* (AN) *on the absorption spectra of solutions* (0·02M) *of vanadous sulphate* (VSO_4) *in* H_2SO_4 (0·3N).



——— Pure solution.
– – – + 1% of $C_2H_3{\cdot}CN$.
..... + 1% of $C_2H_3{\cdot}CO_2Me$.

$E_0 = -21$ v.
$\Delta E_{AN} = 0{\cdot}78$ v.
$\Delta E_{MA} = 0{\cdot}01$ v.

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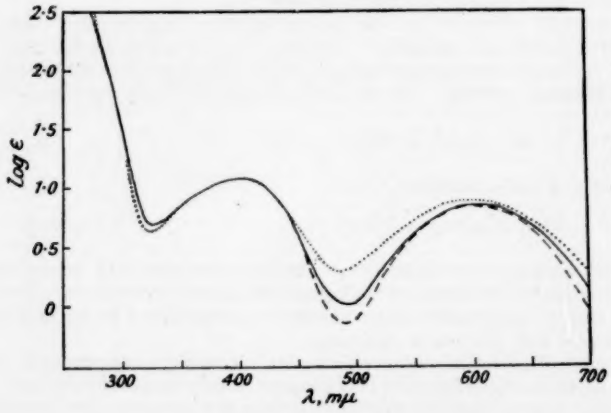
FIG. 3. *The effect of methyl acrylate* (MA) *and acrylonitrile* (AN) *on the absorption spectra of solutions* (0·01M) *of vanadic sulphate* [$V_2(SO_4)_3$] *in* H_2SO_4 (0·3N).



——— Pure solution.
– – – + 1% of $C_2H_3{\cdot}CN$.
..... + 1% of $C_2H_3{\cdot}CO_2Me$.

E_0 (V^{III}/V^{IV}) $= +0{\cdot}31$ v.
$\Delta E_{AN} = +0{\cdot}05$ v.
$\Delta E_{MA} = -0{\cdot}01$ v.

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scopic evidence thus indicates preferential complexing of the monomer with the V^{2+} ion, and in accordance with this it is found that the V^{2+}/V^{3+} redox potential is shifted 0·781 volt by acrylonitrile. As may be seen from Figs. 2 and 3, no such comparable effect is produced by methyl acrylate. Such complexing has a profound influence on the production of free radicals from such ions, which is discussed in the next section.

Methods of Preparation.

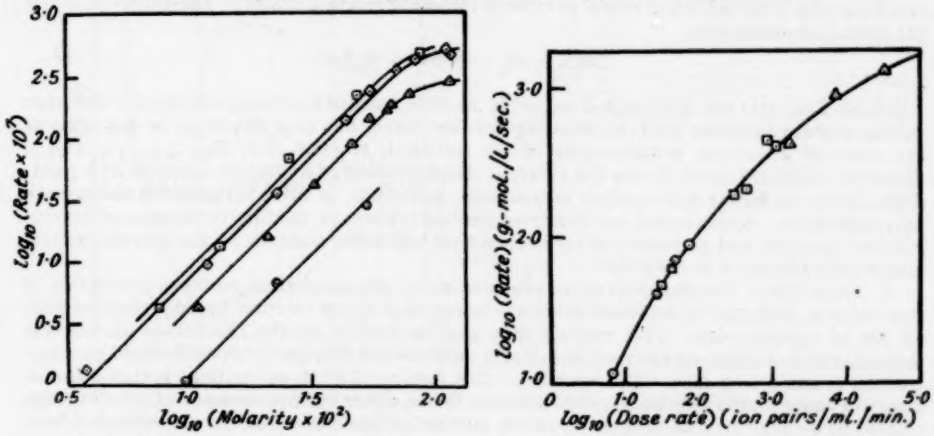
In non-aqueous media free radicals are usually formed by the decomposition of molecules either on surfaces, or homogeneously by heat, light, or other radiation. This is true in aqueous media, where, however, they may also be formed from ions in electron-transfer reactions, in which the solvent plays an important part. It is therefore convenient to discuss the formation under three main headings.

1. *From Molecules.*—The absorption spectrum of dilute solutions of hydrogen peroxide[9] consists of a continuum beginning at ~3800 Å, and absorption of light of any wave-length shorter than this can be shown to cause dissociation into hydroxyl radicals, which may initiate a chain reaction causing the decomposition of the hydrogen peroxide:

$$H_2O_2 \xrightarrow{h\nu} 2OH(^2\pi) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

In the presence of dissolved vinyl compounds no oxygen is evolved, but polymerisation occurs. The polymer can be shown to contain the terminal OH group,[6b] and the kinetics of the reaction

FIG 4. *The polymerisation by X- and γ-rays of acrylonitrile in aqueous solution:* (a) *order with respect to monomer, full lines correspond to second order;* (b) *dose rate dependence.*



(a) □ 40·1 *r*/min. △ 14·7 *r*./min. ◇ 27·3 „ ○ 3·7 „

(b) ○ *Radium γ-rays.* △ 50 *kv.* X-*rays.* □ 220 *kv.* X-*rays.*

at weak extinction suggest that the radicals are evenly distributed throughout the system. In contrast with photochemical systems the absorption of ionising and nuclear radiations is not only non-selective, but the products of the primary act are thought to be formed initially in the wake of the fast charged particles traversing the medium. In the case of water vapour there are substantial arguments for the view that the fast charged particles ionise some water molecules and dissociate others in inelastic collisions. Similar processes would be expected to take place in liquid water,[10] where the net radiochemical reaction might be represented as

$$H_2O_{(l)} \rightsquigarrow H + OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

Confirmation of this view is obtained by irradiation of aqueous solutions of water-soluble vinyl compounds, whereupon the H atoms and OH radicals formed by the action of the radiation on the water initiate polymerisation. It will be recalled that the infra-red evidence proves that both species are effective in this manner. The kinetics of the *X*- and γ-ray-induced polymerisation of acrylonitrile in aqueous solution are illustrated in Figs. 4*a* and *b*, from which it is seen that the rate is proportional to $R^n[m_1]^2$, where R is the dose rate and the exponent varies smoothly from 0·9 at low dose rates to 0·25 at high dose rates and is independent of the wave-length of the radiation used. This result can only be interpreted by assuming that the initiating radicals are not uniformly distributed but are confined to small volume elements randomly distributed throughout

[9] Allmand and Style, *J.*, 1930, 596.
[10] For a detailed discussion see ref. 6(*b*) and Dainton, *Ann. Reports*, 1948, **45**, 5.

the system. In each element the chains undergo radical termination, and the rate in each element is thus $k_i k_p / k'_t [m_1]^2$. At low dose rates, where individual volume elements are isolated from their neighbours, the overall rate should therefore be equal to $kR[m_1]^2$ where $kR < k_i k_p / k'_t$, whereas at high dose rates, above a certain minimum value at which almost every element will be overlapping with its neighbours, the rate of formation of radicals will be uniformly high over the whole system and the reaction rate will be equal to $k_i k_p / k'_t [m_1]^2$. The observed change of the dose rate exponent is taken as evidence of behaviour typical of transition between these two extremes. The fact that a change of wave-length of the incident radiation does not affect the kinetics enables deductions to be made concerning the energy loss of electrons in water which it is inappropriate to discuss here.

Although the photochemical and radiochemical methods of generating radicals in water are associated with different spatial distributions of these species, the system remains single phase in both cases and the radicals are free to diffuse. Recently, Parravano [11] has shown that radicals may be produced in the absorbed phase at metal surfaces. Chemisorbed hydrogen, nitrogen, carbon monoxide, methane, ethylene, and acetylene on different metals, such as nickel, ruthenium, platinum, iron, and osmium were found to initiate the polymerisation of methyl methacrylate in aqueous solution. The efficiency of the initiation is very low, only a small fraction of the adsorbed atoms or radicals initiating reaction chains. The author proposes the initiation mechanism

$$MeX + m_1 \longrightarrow Me + m_1^{\bullet} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

where MeX denotes the chemisorbed radical X, and the order of increasing efficiency of different radical–metal complexes MeX in initiating polymerisation has been shown to be the same as the order of increasing exothermicity of the initiation reaction, *i.e.*, $D_{m_1^{\bullet} \rightarrow m_{1+x}} - D_{Me\text{-}X}$. Similarly, radicals formed during the catalytic decomposition of hydrazine solutions at a palladium surface or formic acid solution at platinum, palladium, or silver surfaces will also initiate polymerisation. Such studies are clearly of general interest in relation to theories of heterogeneous catalysis and of particular interest in that end-group analysis of the polymer should enable the radicals to be identified.

2. *From Ions.*—The discharge of molecular ions provides an obvious means of production of free radicals, and may be achieved either at electrodes or by an electron-transfer reaction with an ion of opposite sign. Free radicals may also be formed by the breakdown of unstable molecular ions of either sign formed from stable molecules by thermal or photochemical electron-transfer reaction with ions. The most important feature of all these reactions is that a simple means of counting the radicals so produced is available, either by measurement of the discharge current or by analytical determination of the number of ions whose state of oxidation has been altered by one unit.

Several workers have observed that cathodic discharge of hydrions at low current densities brings about the polymerisation of dissolved monomers. Parravano [11] has shown that the efficiency of this initiation reaction is low ($\sim 10^{-6}$) but increases with increasing hydrogen overvoltage at the particular metal cathode concerned. This result is readily accounted for by assuming that the initiation reaction is in competition with the recombination of the adsorbed hydrogen atoms.

Interionic electron-transfer reactions have been described by Professor Evans in a previous Tilden Lecture. If the process is purely one of electron transfer and no bonds are broken, the frequency factors for reactions between ions of like sign are generally low, and between ions of opposite sign are generally high. When the spontaneous electron transfer between ions of opposite charge is very slow because the reaction is endothermic, it is frequently possible to achieve it by photochemical means. Several years ago, Rabinowitch and Stockmayer [12] concluded from an examination of the ultra-violet absorption spectra of various salts and bases of multivalent ions that ion-pair complexes of the type $M^{x+}(X^{y-})$ existed in solution with varying degrees of stability, and that the ultra-violet absorption continuum with a high molecular extinction coefficient ($\sim 10^4$) was to be associated with transfer of an electron from the anion to the cation. In the case of the 1 : 1 complexes of ferric ion with univalent anions ($X^- = OH^-$, Cl^-, Br^-, N_3^-, SCN^-, etc.) the electron-transfer process could be represented by

$$Fe^{3+}X^- \longrightarrow Fe^{2+} + X \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

[11] *J. Amer. Chem. Soc.*, 1950, **72**, 3856, and private communication from Professor H. S. Taylor.
[12] Rabinowitch and Stockmayer, *J. Amer. Chem. Soc.*, 1942, **64**, 335.

Evans and Uri [13] have successfully used the polymerisation method to detect the radical X and have proposed the potential-energy diagram shown (Fig. 5) to account for the case of the $Fe^{3+}OH^-$ complex which has a heat of formation of 1·6 kcal. These authors also state that the reaction can be reversed in two ways, a *primary* dark reaction involving the radical and ion formed from the same ion-pair complex, and a *secondary* dark reaction which occurs after separation of the products and does not necessarily involve species formed from the same ion-pair complex. The polymerisation initiation reaction can compete with the secondary reaction only, and when a large excess of monomer is present the secondary reaction is completely suppressed and the true quantum yield of the forward reaction can thus be determined, and is found to be much less than unity. There is still no direct evidence as to the true nature, ionic, $Fe^{3+}X^-$, or covalent,

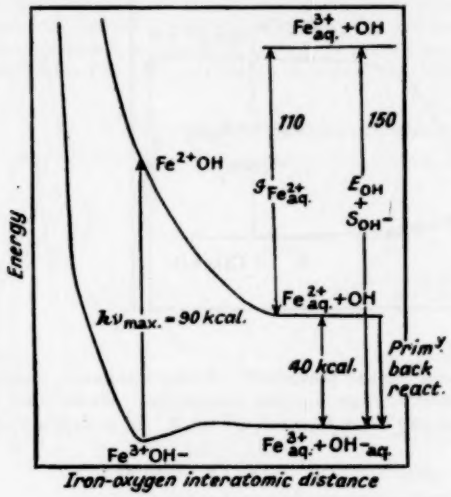


FIG. 5. *The potential-energy curves relevant to the reaction* $Fe^{3+}OH^- \longrightarrow Fe^{3+} + OH$ (taken, by permission, from Evans and Uri, *J. Soc. Dyers Col.*, 1950, 125).

$(FeX)^{2+}$, of such complexes, and the propriety of calling the photochemical process an electron-transfer process has therefore been questioned by Bowen.[14]

When the radical is produced by rupture of a covalent bond, as for example in the formation of OH radicals by Fenton's reagent [15]

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+}OH^- + OH$$

or in the interionic reaction

$$Hg^{2+} + H{\cdot}CO_2^- \longrightarrow H + CO_2 + Hg^+(\tfrac{1}{2}Hg_2^{2+}) \quad . \quad . \quad . \quad . \quad . \quad (17)$$

which James has explored by the polymerisation method,[8] the shape of the appropriate potential-energy curve resembles those for the reaction of sodium atoms with alkyl halides.[16] The essential feature of this diagram (see Fig. 6) is that the Morse curve for the dissociation of the formate ion into $H + CO_2^-$ should be intersected by a repulsive curve between the CO_2 radicals and a hydrogen atom. Intersection will only occur if the ionisation potential of the mercurous ($I_{Hg^+_{aq.}}$) is greater than the sum of the electron affinity of the CO_2 molecule (E_{CO_2}) and the solvation energy of the CO_2^- anion ($S_{CO_2^-}$). In view of the fact that the dissociation energy of the reaction $Hg_2^{2+} \longrightarrow 2Hg^+$ is likely to be low, the value of $I_{Hg^+_{aq.}}$ will be not very different from ΔH for the reaction

$$\tfrac{1}{2}Hg^{2+}_{2\,aq.} \longrightarrow Hg^+_{aq.} + e^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

which can be shown from Brewer's tables [17] to be ~123 kcal. On the other hand, the other quantities, E_{CO_2} and $S_{CO_2^-}$, are unlikely together to exceed this value. The course of the reaction

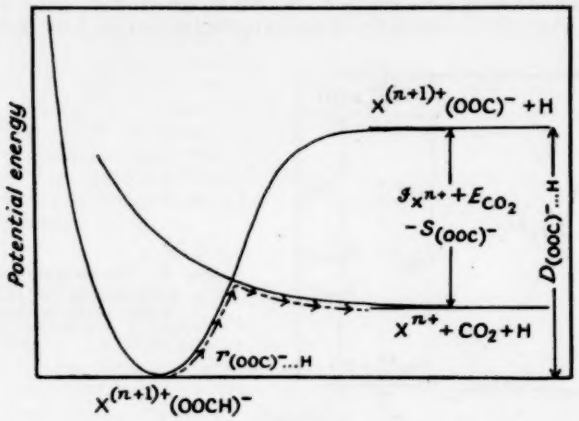
[13] Evans and Uri, *Nature*, 1949, **164**, 404; *J. Soc. Dyers Col.*, 1949, **65**, 709.
[14] Bowen, *Quart. Reviews*, 1950, IV, 236.
[15] *Trans. Faraday Soc.*, 1946, **42**, 155.
[16] Evans and Polanyi, *ibid.*, 1938, **34**, 11.
[17] National Nuclear Energy Series IV—19B, 76 (1950).

is then described by the broken line in the figure, from which it may be seen that a minimum value for the energy of activation is

$$D_{H\ldots CO_2} + E_{CO_2} + S_{CO_2^-} - I_{Hg^+_{aq.}}.$$

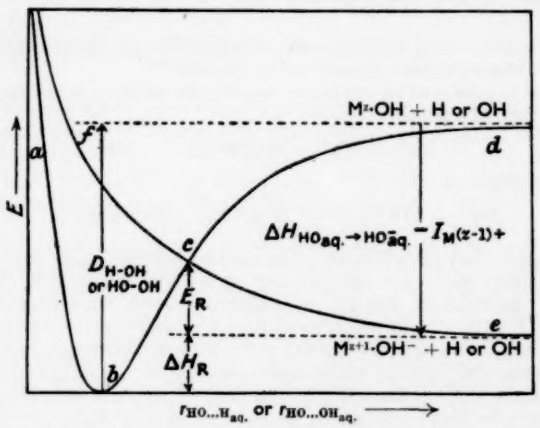
3. *The Special Rôle of Water.*—Attention has already been directed to the influence of the hydration energy of the various ions on the energy of activation of thermal electron-transfer

FIG. 6. *The thermal reaction,* $X^{(n+1)+} + H{\cdot}COO^- \longrightarrow X^{n+} + CO_2 + H$.



reactions resulting in radical formation, and in the magnitude of the minimum quantum necessary in photochemical formation of radicals from ion-pair complexes. Water may also be a reactant in such electron transfer, behaving as an electron acceptor. It is instructive to

FIG. 7. *The reaction* $M^{z+} . HOX \longrightarrow M^{(z+1)+} . OH^- + X$ (X = OH or H).



compare the reduction of H_2O_2 and H_2O by reducing ions. The two reactions may be represented by the equations

$$M^{z+} + H_2O_2 \longrightarrow M^{z+1} . OH^- + OH \quad . \quad . \quad . \quad . \quad . \quad . \quad (19)$$

$$M^{z+} + H_2O \longrightarrow M^{z+1} . OH^- + H \quad . \quad . \quad . \quad . \quad . \quad . \quad (20)$$

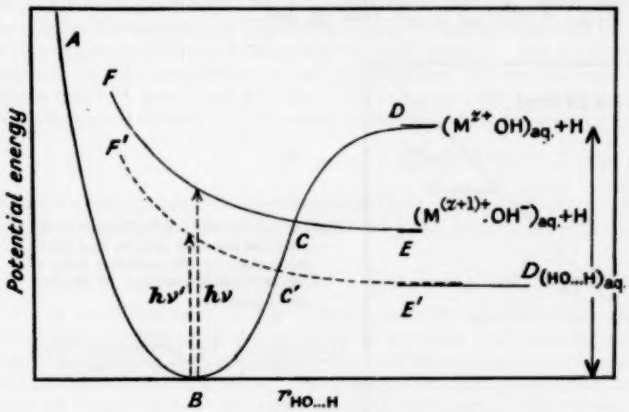
and it is clear that the difference in the heats of these two reactions is merely the difference in the dissociation energies $D(H \ldots OH)_{aq.}$ and $D(HO \ldots OH)_{aq.}$. Both H_2O^- and $H_2O_2^-$ are expected on theoretical grounds to be unstable, and experimental support for this view in the for-

mer case is provided by electron-swarm experiments in water vapour.[18] The general form of the potential-energy curves relevant to the two cases will therefore be the same although the magnitude of the energies concerned will be different. In Fig. 7 we have used one diagram to summarise the course of both reactions, since this permits points of similarity and difference to be emphasised. The conclusions to be drawn are :

(1) The reaction path of the thermal reaction is *bce*, and the energy of activation is $E_R + \Delta H_R$. For the same reducing ion, the energy of activation will clearly be much greater for the fomation of H atoms from water than for the formation of OH radicals from hydrogen peroxide. This is borne out by the fact that when $M^{z+} = Fe^{2+}$, reaction (20) is imperceptible whereas reaction (19) is quite fast, $E_A + \Delta H_R$ being ~10 kcal.[15]

For the *same* reaction, *i.e.*, either (19) or (20), ΔH_R, and hence the energy of activation also, should decrease with decreasing ionisation potential of the reducing ion. There are no quantitative data yet available for testing this, but qualitative observations concerning the stability of reducing ions in water are in accord with this view. For example, whereas Fe^{2+} ions (ionisation potential ~100 kcal.) are stable in water, Ti^{2+} ions (ionisation potential ~72 kcal.) are not.

FIG. 8. *The photochemical electron-transfer reaction,* $M^{z+} . H_2O \xrightarrow{h\nu} M^{z+1} . OH^- + H$.



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(2) When $E_R + \Delta H_R$ is so large that thermal electron transfer is inconveniently slow, absorption of a light quantum may bring about the reaction. Since this process is almost instantaneous it is most effective when the electron donor and acceptor are already closely bound. Photochemical electron transfer from a cation to a water molecule of its hydration shell, with resultant formation of a hydrogen atom, is therefore to be expected with all ions at a suitable wave-length. The appropriate potential-energy diagrams are given in Fig. 8, and for a series of ions of the same valency and size the curves *ABCD* and *FCE* will be substantially the same, but their relative vertical displacement *DE* will be determined by

$$DE = (E_{OH(g)} + H'_{OH^-} - H_{OH}) - (I_{M^{z+}_{(g)}} + H_{M^{z+}} - H'_{M^{(z+1)+}}) \quad . \quad . \quad . \quad (21)$$

where *I* denotes ionisation potential, *E* and *H* denote electron affinity and hydration energy, and the superscript is used to denote only that part of the hydration energy which becomes available during the time taken for the configuration to change from *B* to *E*. The second term on the right-hand side is the only one which is dependent on the chemical nature of the reducing ion, and will probably be slightly larger than the true ionisation potential of the ion in the aqueous environment, *i.e.*, $I_{M^{z+}_{aq.}}$, which is equal to ΔH for the reaction

$$M^{z+}_{aq.} \longrightarrow M^{(z+1)+}_{aq.} + e^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (22)$$

We therefore expect that, in passing from one ion to another in the series of equal valency and size, *DE* and hence $h\nu$ would vary in proportion to changes of $I_{M^{z+}_{aq.}}$ (*i.e.*, $h\nu - h\nu' = I_{M^{z+}_{aq.}} - I_{M'^{z+}_{aq.}}$). Since the entropies of solvation of ions of equal radius and change will be equal,

[18] Crovath, *Physical Rev.*, 1929, **33**, 605.

changes in $I_{M^{z+}}$ will be equal to changes in the redox potential. Mr. James has investigated the electron-transfer spectra of a large number of ions (V^{2+}, Cr^{2+}, Mn^{2+}, Fe^{2+}, Ti^{3+}, Mo^{3+}, U^{4+}, Eu^{2+}, Sn^{2+}, I^-, N_3^-, SH^-, SO_3^{2-}, and $H{\cdot}COO^-$) and the appropriate data for the transition elements of the first long period V to Ni are tabulated below. The expected proportionality between redox potential and the minimum quantum necessary to produce electron transfer is shown in Fig. 9.

The relationship between the minimum value of the quantum for the process $M^{z+}, H_2O \xrightarrow{h\nu} M^{3+} . OH^- + H$ *and the potential of the couple* M^{2+}/M^{3+}, *for ions of approximately the same size.*

Ion	Atomic number	Radius (Å) M^{2+}	Radius (Å) M^{3+}	Redox potentials [1] (volts)	Long-wave absorption edge of electron-transfer spectrum, λ_0, Å	hc/λ_0 (kcal.)
V^{2+}	23	(0·82)	0·69	−0·21	3500 [2]	81
Cr^{2+}	24	(0·80)	0·62	−0·42	3800 [2]	75
Mn^{2+}	25	0·78	0·66	+1·5	2250 [2]	125
Fe^{2+}	26	0·76	0·64	+0·75	2850 [2]	100
Co^{2+}	27	0·74	0·63	+1·8	2200 [3]	129
Ni^{2+}	28	0·73	—	—	2200 [3]	129

[1] Latimer, "Oxidation Potentials," Prentice Hall, 1938. [2] From measurements by D. G. L. James (Leeds). [3] From M. Kasha, *J. Opt. Soc. Amer.*, 1948, **38**, 929.

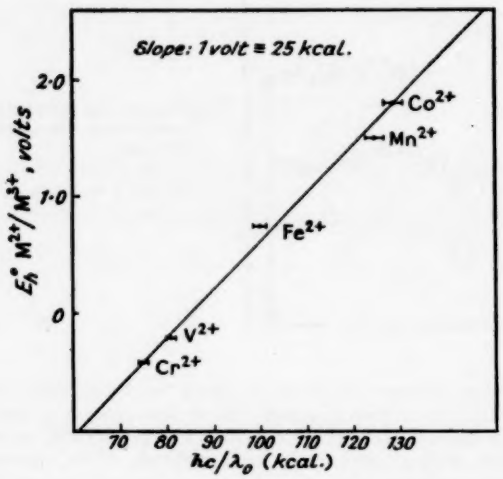

FIG. 9. *The relationship between the electron-transfer spectra and redox potentials of the bivalent ions of the transition elements of the first short period.*

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The effect of formation of a stable complex will be to increase $I_{M^{z+}}$ and cause a shift of the electron-transfer spectrum to shorter wave-lengths. Examination of the spectrum alone may not reveal this effect because additional absorption bands may arise owing to electron excitation within the complex. The wave-length associated with transfer to water and consequent production of hydrogen atoms may be distinguished from the excitation bands by the polymerisation method. An example of this is the addition of acrylonitrile to ferrous sulphate, which produces an extension of the continuous absorption of 800 Å towards *longer* wave-lengths. However, absorption of light in this region is not associated with electron transfer to water since it does not cause polymerisation.

4. *Enzymic Oxidation and Reduction in Aqueous Media.*—The prosthetic group of many enzymes which are catalysts for biological oxidations and reductions, contains a metal element of variable valency, and many authors [19] have from time to time suggested that the intermediates in such reactions might be free radicals. In particular, it is very tempting to regard the hæmoproteins, catalase and peroxidase, which contain ferriprotoporphyrin, as reacting with the hydrogen peroxide which they require to exercise their function, to produce radicals which in the former case lead to a rapid decomposition of peroxide and in the latter case lead to oxidation

[19] For example, Haber and Willstätter, *Ber.*, 1931, **64**, 2844.

of the substrate. This hypothesis is made the more attractive by the fact that mixtures of ferric ion and hydrogen peroxide initiate the polymerisation of dissolved vinyl compounds. However, it has been found [20] that neither catalase– nor peroxidase–hydrogen peroxide mixtures of a wide range of composition initiate polymerisation. Moreover the function of the enzyme is unaffected by the presence of the monomer. It is therefore unlikely that radicals are intermediates in these reactions.

On the other hand, Parravano [11] has shown that during the dehydrogenation of formaldehyde catalysed by xanthine oxidase, which is an enzyme devoid of any metallic element, dissolved methyl methacrylate may be polymerised, provided that the solution is air-free. Although the initiating species has not been characterised, the simplest mechanism would be that the enzyme acts as a hydrogen atom carrier from the formaldehyde to the monomer.

It is curious that in the only enzymic systems investigated, the application of the polymerisation method has produced results which run counter to expectations based on simple ideas of enzyme action.

5. *Oxygen as a Reduction-activation Co-catalyst.*—With the exception of the heterogeneous, photochemical, and radiochemical methods of decomposition, all the methods described above may be classified as " reduction-activation " methods, *i.e.*, involving the interaction of an oxidising and reducing agent. If oxygen could be made the oxidising partner in such a reduction-activation system, exhaustive deaeration to ensure polymerisation would be unnecessary since the molecular oxygen concentration would be maintained at a very low level by a reaction in which polymerisation-initiating radicals were formed. The reducing partner would be the more effective in this reaction the lower its ionisation free energy, and in accord with this we have found that V^{2+}, Mo^{3+}, and U^{3+} form effective reduction-activation systems with oxygen.[21] This is easily demonstrated in the case of vanadium where the overall reaction may be written

$$V^{2+} + O_2 + H_2O \longrightarrow VO^{2+} + 2OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (23)$$

These reactions undoubtedly proceed in single electron-transfer steps involving H_2O_2 as an intermediate, as may readily be demonstrated when oxygen is bubbled through solutions of UCl_3.

The Properties of Free Radicals in Aqueous Solution.

The usual reactions of free radicals, such as combination, disproportionation, addition to unsaturated compounds, will occur in an aqueous environment, but surprisingly little quantitative information has been obtained about them, and in some cases even the precise nature of the products is still unknown. Thus, there is much discussion as to whether, when two hydroxyl radicals react, H_2O_2 or H_2O and O are the products. The former reaction would be expected to have a low frequency factor and an energy of activation determined by the (unknown) dipole repulsion as the reactants approach, whilst the latter would have a normal frequency factor and an energy of activation of about 7 kcal. The behaviour of dilute solutions of hydrogen peroxide at high light intensities suggests that H_2O_2 is not the product,[22] whereas equally strong evidence to the contrary is provided by the fact that H_2O_2 is always formed by the action of α-rays on deaerated water.[23]

Oxidation and Reduction by Radicals.—The reduction potentials on the hydrogen scale for many hypothetical gaseous atoms or radicals in aqueous solution of normal acidity can readily be calculated. Two important examples are

$$H_g \longrightarrow H^+_{aq.} + e^-, \; E^\circ = 2{\cdot}11 \text{ v} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (24)$$

$$HO_{aq.}^- \longrightarrow HO_g + e^-, \; E^\circ = -2{\cdot}85 \text{ v} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (25)$$

(U.S. convention with regard to sign, data taken from National Bureau of Standards " Selected Values of Thermodynamic Quantities ") and these potentials are the quantitative expression of the reducing power of H and oxidising power of OH in simple electron-transfer reactions. It is therefore expected that when H atoms are formed in a medium containing solutes of lower oxidation potential, the H atom will be oxidised; and similar arguments would apply to oxidation reactions by OH. For example, we know that

$$Fe^{2+}_{aq.} \longrightarrow Fe^{3+}_{aq.} + e^-; \; E^\circ = -0{\cdot}77 \text{ v}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (26)$$

[20] Dainton and Smith, to be published.
[21] Dainton and James, unpublished data.
[22] Lea, *Trans. Faraday Soc.*, 1949, **45**, 81.
[23] Bonet-Maury and Lefort, *Nature*, 1948, **162**, 381.

and hence in normal acid solution the reactions

$$Fe^{2+}_{aq.} + OH_g \longrightarrow Fe^{3+}_{aq.} + OH^-_{aq.}; \quad \Delta G^\circ = -48 \text{ kcal.} \quad . \quad . \quad . \quad (27)$$

$$Fe^{3+}_{aq.} + H_g \longrightarrow Fe^{2+}_{aq.} + H_g^+; \quad \Delta G^\circ = -50 \text{ kcal.} \quad . \quad . \quad . \quad . \quad (28)$$

will be associated with a decrease of free energy and should take place spontaneously. Reaction (27) is well known. It is the second reaction which is involved in the oxidation of ferrous ions by hydrogen peroxide. It is also the reaction responsible for keeping the quantum yield for the formation of hydroxyl radicals from $Fe^{3+}{\cdot}OH^-$ complexes at such low values.[13] Likewise, reaction (28) is responsible for maintaining the quantum yield of the formation of H atoms from ferrous ion in water very much less than unity. The potential-energy changes undergone in this reaction may be seen by following the reaction path *ecb* in Fig. 7, from which the relation of ΔH_R and E_R (the energy of activation for this reduction) to the ionisation potential of the ferrous ion may be clearly perceived.

Fig. 7 is also illustrative of a rather surprising possibility, namely, that the hydroxyl radicals might act as a reducing agent, in a reaction which is essentially the reverse of the first stage of the Fenton reaction, *i.e.*,

$$M^{(z+1)+}.OH^- + HO \longrightarrow M^{z+} + H_2O_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (29)$$

and for which ΔG° may well be negative when the redox potentials $M^{z+}/M^{(z+1)}$ is large and negative. Reduction by hydroxyl radicals would be favoured by increasing pH, and Haissinsky, Lefort, and Le Bail [24] have suggested that this reaction can actually occur when $M^{(z+1)+} = Ce^{4+}$.

Another possibility in which H atoms play a rather unusual rôle, has been put forward by Weiss,[25] who suggests that in acid media an equilibrium:

$$H + H^+_{aq.} \rightleftharpoons H_2^+{}_{aq.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (30)$$

is capable of yielding significant amounts of the hydrated molecular ion H_2^+ which, as an electron acceptor, would be a powerful oxidising agent. Although theoretical arguments may be advanced against this notion, yet it should be noted that there is one quite strong piece of experimental evidence for it. Douglas and Yost [26] have found that the quantum yield for the photo-oxidation of europous ion by water exceeds unity. The primary act is

$$Eu^{2+} + H_2O \xrightarrow{h\nu} Eu^{3+}OH^- + H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (31)$$

and a quantum yield for this process exceeding unity is unlikely. There must therefore be another oxidation step, and the obvious possibility is

$$H + H^+ + Eu^{2+} \longrightarrow Eu^{3+} + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (32)$$

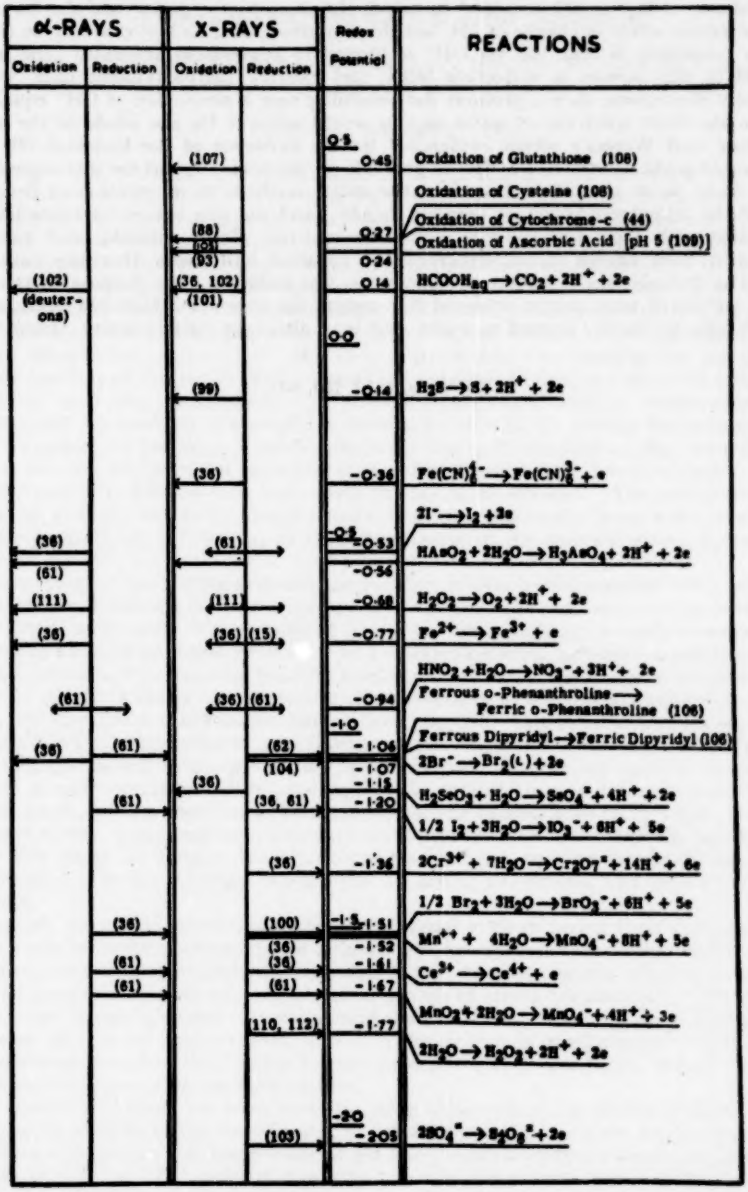
but whether there is a termolecular process as written, or a bimolecular one between $Eu^{2+} + H_2^+$ or $Eu^{2+}.H + H^+$ cannot be determined.*

It was stated earlier that the net radiochemical act in liquid water was to form an equimolecular mixture of H atoms and OH radicals. The reversible redox potential of such a solution when acid ought to be −0·37 volt, and it would be expected that, provided the electron-transfer reactions involved are reversible thermodynamically, irradiated water would act as an oxidising agent towards all systems of smaller or positive redox potential and as a reducing agent towards those systems which possess more negative redox potentials. In Fig. 10 we have arranged all the known *X*- or α-ray-induced reactions which occur in water, with the exception of the bleaching of dyes, in order of their redox potentials and have indicated whether oxidation or reduction occurs.[27] Whilst it is obvious there are two fairly well-defined zones of oxidation and reduction and that the assignment to irradiated water of an "equivalent redox potential" (E.R.P.) is justified, the figure shows unmistakably that the observed value (∼−0·9 v) is not that expected (−0·37 v). Several modifications of the simple theory can be suggested which, in some degree at least, would account for the anomalously high oxidative capacity. The first is that the hydroxyl-radical concentration exceeds the hydrogen-atom concentration. This irregularity has always been assumed for other reasons, and is more marked the greater the linear ion density in the

[24] *J. Chim. physique*, 1950, **48**, 210; *Compt. rend.*, 1950, **230**, 1156.
[25] *Nature*, 1950, **165**, 728. [26] *J. Chem. Physics*, 1949, **17**, 1345.
[27] Collinson and Dainton, *Ann. Rev. Phys. Chem.*, 1951, **2**, 108.

* [*Note added in proof.*] Douglas and Yost (*J. Chem. Physics*, 1950, **18**, 1687) have now stated that the quantum yields given in their paper [26] are too large by a factor of ten. It is therefore no longer necessary to invoke reaction (32) to account for their results.

FIG. 10. *The equivalent reduction potential of irradiated water.*



→ *denotes whether oxidation or reduction,* ↔ *denotes equilibrium attained or equivocal data. For meaning of numbers over the arrows see ref.* 28.

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track of the fast charged particle concerned. Calculated values of the ratio [HO]/[H] have, however, never exceeded 10^4, whereas the value required to account for E.R.P. $= -0{\cdot}95$ is $\sim 10^{19}$. The existence of H_3^+ would also tend to reduce the discrepancy, and would also be in accord with the known effect of change of pH, but the magnitude of the effect can only be conjected. Another possibility is that the ion OH^+ is formed in appreciable amounts. The oxidation potential of this species is extremely large, and existing thermodynamic data, which are admittedly incomplete, do not prohibit the possibility that a proportion of OH^+ equal to that found in the mass spectrum of water vapour would account for the whole of the anomaly. Darbyshire and Waters's recent evidence [28] for the existence of the hydrated OH^+ ion in concentrated acidic solutions of hydrogen peroxide affords some support for this suggestion.

For many years after their discovery, the major methods of preparation of free radicals involved the homolytic fission of covalent bonds; and for this reason chemists have been preoccupied with their behaviour in non-polar systems. Ionic solvents, and particularly water, with their known incompatibility with covalent substances therefore came to be regarded as unlikely media for the production of free radicals. The purpose of the present Lecture will have been partly achieved if it creates the impression that odd-electron species may not only be readily formed in water, but may also take part in many varied types of reaction.

[28] *Nature*, 1950, **165**, 401.

Transient Entities in Chemical Reactions.

LIVERSIDGE LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY AT THE ROYAL INSTITUTION, LONDON, MAY 10TH, 1951.

By H. W. MELVILLE, F.R.S.

THE study of the problem of chemical reactivity has progressed generally by a series of rather discontinuous steps in which new concepts have stimulated much experimental and theoretical work followed by periods of consolidation. In this Lecture there is described one such concept which has been developed especially vigorously since 1945 and has led to a fuller understanding of certain types of reaction in which atoms and radicals play an important part. In any reaction one of the essential pieces of information that must be obtained concerns the nature of the bodies that take part in those collisions leading to chemical transformation. This may seem to be a self-evident truth in simple reactions but in complex reactions the realisation of this fact has not always been appreciated. Not only is it necessary to establish the identity of the reacting species and the products of reaction, but precise information about their effective concentration must also be obtained. In reactions between molecules, whose mechanism is authenticated by methods now available, there is no difficulty in getting the necessary information. Similarly in reactions in solution between ions and molecules or other ions the information is also readily provided since the study of electrochemistry has produced a variety of methods whereby effective ionic concentration may be determined. The reactions mentioned above are, however, extremely simple because only two, and rarely three, bodies are concerned and the products do not in general affect the course of the reaction except by mass-action effects.

Unfortunately, investigations during the past two decades have demonstrated to an increasing extent that reactions are far more complex even although the reactants and products are relatively simple molecules. The underlying reason for this complexity is really economy of effort in carrying out a given transformation. In a reaction between molecules, a sufficiently violent collision serves to loosen certain bonds in a molecule so that at the moment of collision certain atoms or groups of atoms change partners and molecules of the product emerge from the collision, the chemical transformation having been effected. But there is another way in which even the same transformation may be brought about. It is now a well-established fact that an atom or a radical will attack a molecule much more readily than will another molecule. The product of such a reaction will be another atom or radical—maybe different, maybe identical. In due course another molecule is attacked and so the process goes on in which, according to the chain theory, many molecules may be transformed for each radical initially produced. The factor that limits the number of such occurrences is simply reactions which ultimately remove the radicals. The more highly competitive the latter, the smaller the number of molecules attacked.

Another important generalisation has also become evident during these developments. It is that when molecules are decomposed by heating or by exposure to radiation there is a tendency to undergo fission into radicals, because this is the simplest possible mode of decomposition since no complicated movements of atoms or groups of atoms are necessary. Thus, although rather more energy is needed to sever a bond than loosen it, once the radical is let loose many molecules may be induced to react, and thus the process is energetically economical. It is not surprising therefore that, owing to the operation of these principles, radical reactions are very common in non-ionic transformations.

A considerable effort has been made by using well-developed methods of chemical kinetics to prove the validity of the mechanisms, to get a general picture of the kind of reactions that molecules undergo, and in many cases to get fairly reliable evidence about the nature of the radicals involved. Until recently one vital piece of information has been lacking, namely, knowledge of the actual radical concentrations. If this knowledge is available it then becomes possible to account for the overall quantitative characteristics of the reaction in a completely satisfactory manner and to predict the course in any given circumstances. It is this particular aspect of the subject that will be dealt with in this Lecture. There are many lines of approach, some of which were developed just before the War; others have been extensively developed only during the past few years and progress is still rapid.

Direct Methods.

Normally, radical concentrations in the liquid phase do not exceed about 10^{-7} mole/litre, and in the gas phase about 10^{-3} mm.; hence direct measurement of radical concentration is impossible. With the very much less reactive radicals of the triphenylmethyl type much higher concentrations may be obtained, and the concentration can be determined either from measurement of the paramagnetism of the system or by observations on the rate of conversion of para-hydrogen bubbled through the solution. The unreactivity of such radicals, however, makes this method very restricted indeed.

Another direct spectroscopic method is useful and by certain modern developments has come into consideration as a very promising possibility, especially in the gas phase. Some twenty years ago it was observed that, when water vapour is heated to a sufficiently high temperature, the absorption spectrum of the hydroxyl radical can actually be observed, thus demonstrating the existence of the equilibrium $H_2O \rightleftharpoons H + OH$. With modern developments in intense sources of radiation the spectroscopic detection of radicals has become a possibility (Porter, *Proc. Roy. Soc.*, 1950, *A*, **200**, 284). In order to get sufficiently high concentrations of radicals, a brief flash of radiation may be conveniently produced by discharging a condenser through a suitable tube containing krypton or xenon. Flashes of energy content of the order of 1000 joules lasting for about 10^{-5} sec. are sufficient completely to decompose simple molecules like hydrogen sulphide. If the reaction tube is so arranged that an absorption spectrum of the gas during the period of discharge is obtained, it is in principle possible to detect those radicals having a well-defined absorption spectrum. The necessary intense and brief source of radiation is also provided by a flash tube. In this way simple diatomic radicals like HS and S_2 may be detected during the decomposition of H_2S. Furthermore, by mechanical methods exposures may be made after the source of decomposing radiation is cut off, so that some idea of the life-time and therefore reactivity may be obtained. Although the method is confined to the gas phase and to relatively simple radicals, it is applicable to a great variety of reactions in which knowledge even of this kind of radical is entirely lacking.

Indirect Methods.

All the other methods which have been devised are really indirect although they are completely valid. In any reaction occurring steadily the rate of radical production (I) must always be equal to the rate of radical removal. If only one kind of radical is involved in the rate-determining step of the reaction and such a radical disappears by interacting with another of its kind, then $I = kP^2$ and $P = (I/k)^{\frac{1}{2}}$. There is a further simple relation, namely, $P = I\tau$. Hence if we can measure the rate of production of radicals and their life-time (τ), all the necessary information is at once available to obtain a complete analysis of reaction mechanism.*

Determination of the Rate of Production of Radicals.—The accurate determination of I is not an easy matter but methods have been evolved over a long period. One method consists in the measurement of the length of an induction period when a specified amount of inhibitor is added. It is then assumed that all the radicals initially produced interact chemically with the inhibitor, which is likewise destroyed. The rate of consumption of inhibitor is then computed from its initial concentration and the duration of the induction period. Two important conditions need to be fulfilled—the inhibitor should not affect radical production, and the product of reaction should be inert in so far as the reaction itself is concerned. Alternatively, a retarder is added in such a concentration that the reaction chains are wholly stopped by chemical interaction with one of the radicals propagating the chain. The rate of consumption of the retarder, which may be measured by various methods, then gives the rate of production of radicals. In polymerisation there is, fortunately, a very direct method provided conditions are chosen suitably. In vinyl polymerisation each radical that induces polymerisation produces one polymer molecule. The number of polymer molecules may be conveniently counted by osmotic-pressure determinations and hence the rate of radical production may be computed.

The Determination of Radical Life-times.—The determination of the life-time of radicals is a much more complex matter for, in general, these are usually short, anything from 10^{-3} to 10^{2} seconds. Many methods are now available for this determination, and the main theme of this Lecture is to describe some of the methods that have been devised to solve this question. The problem can be approached in this way: Suppose we consider one of the simplest radical reactions, namely, addition polymerisation in which the repeating reaction is the addition of a

* When two or more radicals are involved in the rate-determining steps the problem can also be oslved though the analysis becomes much more complicated.

monomer molecule to a polymer radical to make a bigger polymer radical. In this way, starting with a small radical, as many as 10 000 molecules of monomer may be added on to such a radical. Further, suppose that small radicals are suddenly produced in the monomer medium, *e.g.*, by radiation with ultra-violet light, then if we plot radical concentration as a function of time (Fig. 1), the curve will rise at first linearly but will soon fall off since radicals will tend to combine with each other until a steady state is reached in which radical production and removal are equal. Now the rate of reaction is proportional to the radical concentration, so another curve (Fig. 2) may be drawn showing the amount of reaction as a function of time. It will be seen that a finite time is required for the reaction to go steadily. In this so-called non-stationary state the radical concentration is increasing to a steady value. Similarly, if the light is cut off the reaction will continue in the dark at a decreasing speed. On the assumption that there exists means whereby these curves may be delineated, the problem is how to calculate precisely the

FIG. 1. *Radical concentration–time curves in a photochemical reaction.*

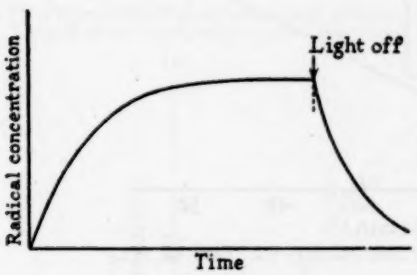
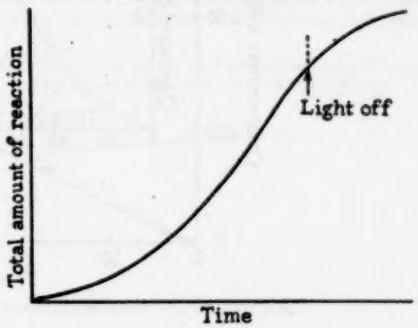


FIG. 2. *Total amount of reaction–time curves for photochemical reactions.*



life-time of the radicals when the reaction is going steadily. During the non-stationary period the net rate of production of radicals is given by

$$\mathrm{d}P/\mathrm{d}t = I - k_t P^2$$

(This will of course become zero when the steady state is reached.) The total amount of reaction that will have occurred up to time t is proportional to

$$\int \mathrm{d}P = \text{const.} \int_0^t (I - k_t P^2)\mathrm{d}t$$

where the constant is calculable from the nature of the reaction. On integration of this equation it may be shown that the fractional amount of reaction $\Delta M/M$ is given by

$$\frac{\Delta M}{M} = \frac{k_p}{k_t^{\frac{1}{2}}} I^{\frac{1}{2}} t - \frac{k_p}{k_t} \ln 2$$

where k_p is the reaction coefficient for the interaction of a polymer radical with a monomer molecule. There is thus at high enough values of t a linear relationship between $\Delta M/M$ and t with a slope of $k_p/k_t^{\frac{1}{2}} I^{\frac{1}{2}}$ and an intercept on the time axis of $(k_p/k_t) \ln 2$. The ratio of slope to intercept is $k_t^{\frac{1}{2}} I^{\frac{1}{2}}/\ln 2$, and since I is known k_t may be calculated and so the value of the life-time may be determined. Similarly, the value of k_p may be calculated and therefore all the detailed information about quantitative radical reactivity at once obtained, for the effect of temperature on k_p and k_t may be easily determined.

No chemical method for this delineation is applicable because of the time limitation, and therefore physical methods alone must be employed. In almost any chemical reaction there is a change in the physical properties of the system. The problem here is to develop physical methods of the requisite sensitivity and such that records may easily be obtained. The following methods have proved suitable for this purpose: dilatometry, dielectric-constant change, refractive-index change, temperature and viscosity changes. Each method has its particular virtues and defects but together they cover at present every reasonable requirement. It is convenient to consider the basis of operation of the methods and the development of suitable instruments for these experiments.

Super-dilatometer.—In an addition polymerisation reaction there may be a contraction of as much as 20%. In a thermostat regulated to 0·01° it is a straightforward matter to detect by this means the formation of 1 part of polymer in 10^3 parts. Further increase in accuracy is limited by the constancy of temperature of the thermostat. In this particular case, however, constancy for a long period is not really necessary (Burnett, *Trans. Faraday Soc.*, 1950, **46**, 772). If one therefore uses a very sensitive dilatometer as a thermometer the surprising result is that in a period of 1 minute the bath temperature may not drift more than 10^{-5}°. Hence a sensitivity of 1 part in 10^7 of volume change may be detected in this interval of time, and the method

FIG. 3. *Course of reaction for photopolymerisation of styrene.*

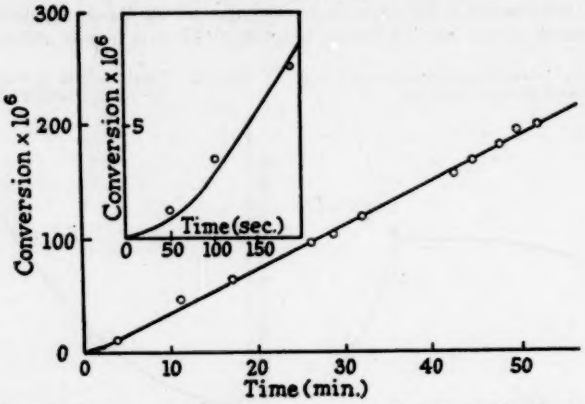


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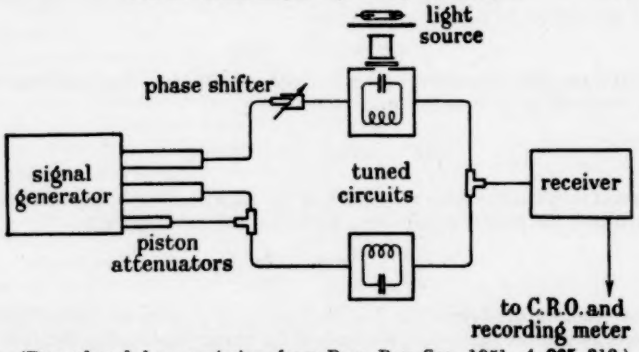
FIG. 4. *Block diagram of the capacity bridge.*



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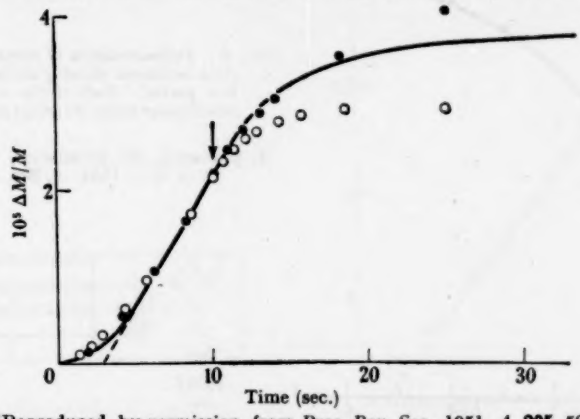
becomes applicable to study the problem. Unfortunately, polymerisations and oxidations are exothermic reactions and hence the temperature of the reaction system may rise, giving a volume increase as opposed to decrease that occurs in polymerisation. The heat must be conducted away more rapidly than would normally occur through the glass walls of a dilatometer. This can conveniently be done by introducing liquid mercury into the dilatometer. Fig. 3 shows the result when the amount of reaction is plotted against time for the photopolymerisation of styrene. It will be seen that the true induction period of the reaction is well displayed, and the extrapolation of the straight line when the steady state of the reaction is established gives an accurately measurable intercept on the time axis.

Dielectric-constant Method.—It is safe to say that in almost any reaction there will be a change of dielectric constant. Again, if we consider polymerisation the general rule is that the polymer has a higher dielectric constant than the monomer. In order to get the maximum

possible sensitivity for an instrument, it is convenient to operate at a frequency of the order of 100 Mc./s. To achieve the necessary sensitivity a very special design of bridge circuit is required. The principles of operation can most readily be seen from a block diagram (Fig. 4) of the electrical circuit of the instrument (Majury and Melville, *Proc. Roy. Soc.*, 1951, *A*, **205**, 309). The signal generator is constructed in such a way that two separate outputs are derived from it, the two output voltages being 180° out of phase. The two output voltages are made nearly equal by means of a device known as a piston attenuator in which a small receiving aerial may be moved up and down a brass tube. A third auxiliary attenuator is fitted so as to provide a fine adjustment for the equalisation of output voltage. By this means the voltages are made equal to within 1 part in 10^8 parts. These two signals are transmitted by means of co-axial lines to each of two oscillating circuits which are precisely identical mechanically and electrically. In order to ensure that the voltages be 180° out of phase, a slight alteration is made in the length of one-axial cable. Since the wave-length used is about 6×10^2 cm., an alteration of 10^{-3} cm. in length gives a very precise means of adjustment. Any signal received from the oscillating circuit is reunited and fed to a suitable amplifier, rectified, and displayed on a voltmeter, cathode-ray oscillograph, or pen recorder. The capacity of the circuit consists of a flat silica cell which

FIG. 5. *Polymerisation of methyl acrylate, showing natural induction period and photochemical after-effect. The full circles correspond to second-order decay of radicals; the open circles to first-order decay.*



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is filled completely with the monomer to be investigated. A hole is cut in the side of the box to admit radiation to the cell. Fortunately, although light gets in, electromagnetic radiation does not get out. If now the whole circuit is energised and the cell in one arm of the bridge illuminated, polymerisation is induced and the dielectric constant will change. The result is that the frequency of oscillation is slightly altered and a signal is produced at the T-junction of the bridge. This signal is displayed on the cathode-ray tube. On switching on the radiation, a time base circuit is also brought into action and hence the change of dielectric constant as a function of time is displayed on the screen and photographed in the ordinary way. By this method it proves possible to detect 1 part in 10^8 of change in dielectric constant in 10^{-3} second. When the experiment is done the most surprising result is that the dielectric constant *decreases* instead of increasing. Four factors can, however, contribute to the change in dielectric constant. First, infra-red and ultra-violet radiation absorbed by the system can raise the temperature and so decrease the dielectric constant: these can be eliminated by suitable filters. Radical production may be inefficient, which means that radiation is degraded to thermal energy: efficient photosensitisers combined with a long chain length can minimise this effect. Then, since polymerisation is exothermic and since, moreover, such measurements can be made in very short intervals of time, the heat so generated stays in the reaction system, causing the liquid to expand and so to lower the dielectric constant: the reaction is therefore carried out adiabatically. When the calculations are made it turns out that the dielectric constant decreases owing to the adiabatic character of the reaction being greater than the increase due to polymerisation. The net result is therefore a decrease when liquid completely fills the reaction cell.

In flat cells of a thickness of 5 mm., half the heat in the cell escapes in about 60 seconds under normal conditions. In effect therefore the instrument is a recording thermometer. It may be shown that the temperature sensitivity is 10^{-5}° and that it is an easy matter to measure an amount of heat as small as 10^{-3} calorie generated in any time up to 60 seconds. Even a direct measure of the quantum yield of the reaction can also be made. By using the appropriate photosensitiser of the polymerisation in an inert liquid like benzene, the instrument can be used as a radiometer to measure the total energy absorbed by the system. The quantum yield is directly calculable, since the wave-length of the activating radiation is known.

Fig. 5 shows how the amount of polymerisation varies with time. It will be seen that there is a period of induction followed by steady reaction, and a decay when the light is switched off. This permits the intercept to be accurately determined and therefore the average life-time of the reaction chain. It is of interest to consider the decay curve. This might follow a first-order law, *i.e.*, the radical interacts with a molecule, or a second-order law, *i.e.*, radical–radical interaction. These two relationships are drawn in Fig. 5, and it will be seen that the results conform much more closely to the second-order law, giving a direct indication as to how the radicals

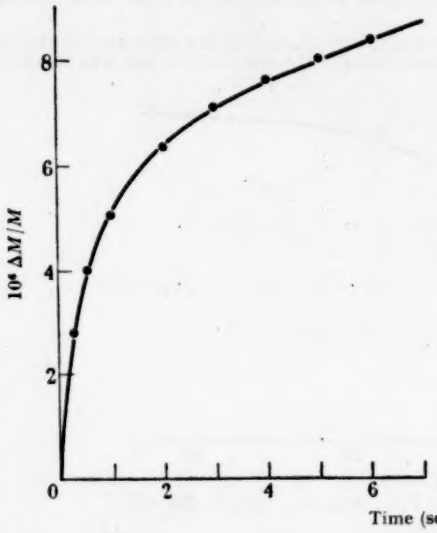

FIG. 6. *Polymerisation of vinyl acetate with flash technique showing absence of induction period. Full circles correspond to bimolecular decay of radical concentration.*

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disappear. This method may also be used in quite a different way. Instead of continuously illuminating the system during the non-stationary phase, we may make use of high-intensity flash tubes giving a pulse of radiation lasting a time much shorter than that of the reaction chain. A krypton discharge tube with a flash time of 10—100 microseconds is convenient for this purpose. The result of using such a technique is that many small radicals are produced simultaneously in the vessel. These then start to grow as polymer radicals, their concentration gradually decreasing as they interact with each other. In this case, as Fig. 6 shows, there is no induction period because the steady concentration is in a way established right at the start of the reaction. The initial slope of the trace is thus a direct measure of the rate of molecular growth (although, of course, many molecules are growing at the same time). One might with reason say that molecules can be seen growing. A theoretical bimolecular curve is shown alongside the experimental points, and it will be seen that the decay accurately follows the bimolecular law. The constants of this bimolecular decay curve enable the average life-time of the radicals to be computed.

Recording Interferometer.—Another physical method which in principle is suitable for study of the non-stationary state is the change of refractive index. To get the necessary sensitivity an interferometer technique is essential to detect a change of 1 part in 10^7 parts. The Jamin type of interferometer is the most suitable for it can conveniently be modified as a recording instrument to work in short time intervals (Grassie and Melville, *Proc. Roy Soc.*, 1951, *A*, **207**, 285). The principles of operation are shown by Fig. 7. An intense source of radiation illu-

minates the slit, and the beam is split by a glass block. The two beams pass through two tubes which form the reaction system. The beams are reunited by another glass block, giving rise to an interference pattern. Both tubes are filled with monomer, and reaction is induced in one by radiation, the other serving as a compensator. As a result, the fringe pattern moves past a reference point and the rate of movement may be observed visually or, if it is fast, by means of a cinema camera. Fig. 8 shows the movement of the fringes as a function of time, the movement indicating a *decrease* in refractive index. It is, however, a general rule that the refractive index of a polymer is greater than that of the monomer from which it is derived. The explanation of this apparent anomaly is similar to that in the dielectric-constant method, namely, that the reaction is mainly adiabatic. The resultant small temperature increase causes a decrease in refractive index which more than compensates for the increase due to polymerisation. It will be seen that there is again a finite induction period before a steady rate of reaction is attained. Consequently, the average life-time of the reaction chain may be obtained by means of the theory mentioned above. The method is not so sensitive as the dielectric-constant change, but it has the merit that the reaction system need not be an organic liquid with a relatively low dielectric loss.

FIG. 7. *Interferometric method of following polymerisation in the non-stationary-state.*

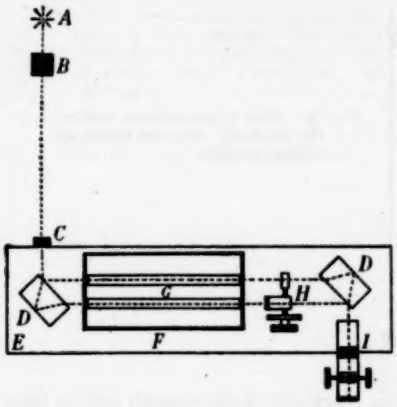

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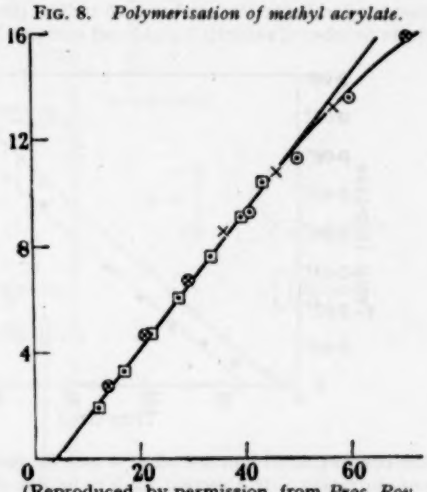
FIG. 8. *Polymerisation of methyl acrylate.*



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Recording-thermometer Method.—The results with the dielectric-constant and interferometer methods suggest that the most direct way of following the non-stationary state of reactions is to use some direct recording thermometer which must be sufficiently sensitive, and to arrange conditions so that the reaction is adiabatic. This has become possible by recent developments of direct-current electronic amplifiers. The experimental arrangement simply consists in suspending a tungsten wire down the axis of a dilatometer tube, the wire forming part of a balanced bridge (Ross, unpublished experiments). The out-of-balance current produced when polymerisation is induced photochemically is amplified and recorded on a suitable scale. Provided the experiment is not continued for longer than 1 minute, conditions in the centre of the tube are substantially adiabatic, and hence, if the heat of polymerisation and the specific heat of the monomer are known, the temperature increase gives a direct measure of the amount of reaction that has occurred. Fig. 9 shows the increase in temperature during the polymerisation of methyl acrylate, the curve being of a similar shape to that with the other non-stationary state method.

Viscometry.—The non-stationary state in a polymerisation reaction may be studied in another, less direct fashion. The viscosity of a monomer undergoing polymerisation is very markedly increased by the addition of relatively small amounts of polymer, and the higher the molecular weight the more marked is the increase. When polymerisation is proceeding steadily the viscosity of the system increases according to a complex relationship which depends, not only on

the rate of production of polymer molecules, but also on their molecular weight and concentration. If the reaction is initiated photochemically and the light is cut off, the viscosity goes on increasing in the dark, but at a diminishing rate (Bamford and Dewar, *Proc. Roy. Soc.*, 1947, *A*, **192**, 309). This is due to the diminution in radical concentration as they interact with each other. Although viscometric measurements can only be made relatively slowly, if the reaction rate is small enough radical life-times can be made very large—many minutes—so that there is no difficulty in observing viscosity as a function of time. Although the analysis of the results is not easy, this kind of photochemical after-effect may be used to calculate velocity coefficients.

Sector Method.—The first method developed to measure the absolute reactivity of radicals was that of the so-called rotating sector (Burnett and Melville, *Proc. Roy. Soc.*, 1947, *A*, **189**, 456). Here, intermittent radiation is used, and the rate of reaction is a function of the time between the flashes of radiation. The effect of intermittency was discovered in 1926, but it was not until 1940 that it was shown how, by combining this effect with other kinetic data, absolute reactivity of radicals could be obtained, and the first measurements of any accuracy were not made until 1945. This method is much less direct than that of the non-stationary state, but it is easy to use and needs no elaborate equipment. The only essential is that the radicals disappear mainly by interaction with each other. The principle of the method is simply the temporal interference between radical production during the flashes of radiation. When a finite number of radicals is produced during a brief flash, then in the following period of darkness

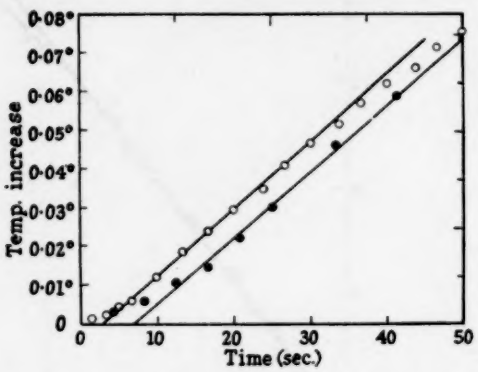

FIG. 9. *Rise of temperature during the adiabatic polymerisation of methyl acrylate.*

the concentration will fall off at a rate depending on the reactivity of the radicals and on their concentration. If a second flash is produced before the first lot of radicals has disappeared, then the second crop of radicals will interfere with the first lot and alter the decay period. It has already been seen that considerable effort must be made to follow such phenomena in the non-stationary state methods. The sector method possesses the great advantage of integrating the effect over many cycles of light and dark; therefore relatively simple methods of following the reaction may be used. It is, of course, restricted to reactions in which radicals disappear two at a time, and this fact makes it essential to have other methods available, for there are in fact quite a large number of reactions in which radical disappearance is a first-order reaction. The reason for this behaviour is the transformation, by collision with a molecule, of a reactive radical into a highly stabilised radical.

Spatial Interference.—The principle of temporal interference may be extended to provide another method of spatial interference which is applicable in both the gas and the liquid phase. In the gas phase this is done in the following manner (Jones and Melville, *Proc. Roy. Soc.*, 1940, *A*, **175**, 392). If a narrow pencil of radiation is projected into a reaction vessel, reaction will occur not only in the illuminated zone but will spread out into the surrounding unilluminated zones to an extent that will depend on the life-time of the radicals. Further, if it were possible to explore radical concentrations spatially, the life-time could readily be calculated from the diffusion coefficient of the radicals, but this is experimentally a very difficult problem to solve. The principle of interference, however, can be utilised to obtain the necessary information. A second similar beam is projected into the vessel parallel to the first. If these beams are far enough apart the radicals in the two reactive zones will not interfere. When the beams are brought closer together so that the zones overlap, interference will occur and there will be an

overall drop in the velocity of the reaction. Thus the rate of reaction is a function of the distance between the two beams of radiation. By appropriate analysis, the life-time of the radicals may be calculated. Even in the liquid phase this principle may be used to get some idea of the distribution of radical concentrations, since convection currents so disturb the distribution of radicals that it is impossible to make the calculations even though radical reactivity is known (Burnett, Valentine, and Melville, *Trans. Faraday Soc.*, 1949, **45**, 960). In this case it is convenient to employ two similar sources of initiating radiation on either side of a reaction vessel. If the radicals are confined to a zone close to the wall of the vessel there will be no interference; on the other hand, if the radicals are uniformly distributed throughout the vessel there will be complete interference. Once more, the rate of reaction will be dependent on the distribution of radical concentration, and the extent of the distribution of radical concentration and the extent of the distribution may be explored by this interference method.

Spatial Competition.—The above-developed methods are particularly applicable to chain reactions—oxidations, polymerisations, etc.—but there are many reactions of different types

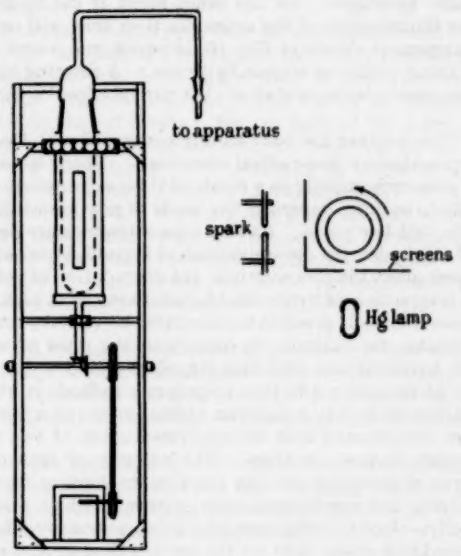

FIG. 10. *Arrangement to measure life-time of NH_2 radicals. The spark decomposes the ammonia, and the mercury lamp decomposes the hydrogen.*

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where these methods would be inapplicable. In the gas phase a simple example is the addition of a hydrogen atom (the simplest radical) to an olefin, for example, ethylene. Here another principle may be invoked. If matters can be so arranged that there are two competing reactions for a given radical, the extent of the competition is known and the absolute velocity of *one* of the reactions is known or is calculable, and the absolute velocity of the other may of course be calculated. This can be done in the following fashion (Robb and Melville, *Proc. Roy. Soc.*, 1949, *A*, **196**, 445). A convenient competitive reaction is the interaction of atomic hydrogen with solid molybdenum oxide. If in a reaction vessel atomic hydrogen is generated photochemically (*e.g.*, by photosensitisation with mercury vapour) and at the bottom of the vessel there is a layer of molybdenum oxide, then the geometry of the system can be so arranged that all the hydrogen atoms produced reach and are absorbed by the oxide. If now ethylene is introduced at such a pressure that an appreciable fraction of the atoms is captured by the ethylene, then fewer atoms will be taken up by the oxide. The uptake of atoms by ethylene can be measured by micro-analytical methods. A more convenient method makes use of the fact that molybdenum oxide goes blue on absorbing hydrogen atoms. The blue colour can be measured photometrically and this provides a far more sensitive means of following the reaction. The surprising fact is that the ethyl radicals are also absorbed quantitatively and give rise to a blue colour. Fortunately, the rate of development of blue colour with ethyl radicals is less than that due to atomic hydrogen so the introduction of ethylene results in a decrease of this rate. Owing to

the simplicity of the geometry of the system and to the fact that boundary conditions are precisely known, accurate diffusion calculations can be carried out and the velocity coefficient can be evaluated. This technique enables many fast reactions to be measured with collision efficiencies up to 1×10^{-3}. It is of general applicability with atomic hydrogen because many alkyl radicals have blueing coefficients significantly different from those of atomic hydrogen. Occasionally, alkyl radicals have the same blueing coefficient as that of atomic hydrogen, but fortunately tungsten oxide is also useful in this connection and the blueing coefficients are then significantly different.

Finally, there is another type of interference method in which one radical is made to catch the other (Birsi and Melville, *Proc. Roy. Soc.*, 1940, *A*, **175**, 187). If ammonia is decomposed photochemically, NH_2 and hydrogen atoms are the primary products. In presence of excess of atomic hydrogen produced independently by mercury photosensitisation, recombination to ammonia occurs and thus hydrogen atoms are inhibitors of the decomposition. If, however, the source of hydrogen atoms is not switched on until an appreciable time after the NH_2 has been illuminated, then there is no inhibition because there are no NH_2 radicals to react with atomic hydrogen. On the other hand, if the hydrogen atoms are generated quickly enough after illumination of the ammonia then they will catch the NH_2 radicals. This is done by the arrangement shown in Fig. 10, in which one source of radiation decomposes the ammonia and the other produces atomic hydrogen. A rotating shutter permits the interval between the two processes to be regulated so that the life-time of the NH_2 radical can be determined.

This Lecture has been mainly concerned with the development of new methods for the study of quantitative free-radical chemistry. There is no time or space to discuss the results which are mounting rapidly as a result of these advances in chemical kinetics. But perhaps it is worth while to indicate generally the kinds of new knowledge that have become available in the course of the last few years. Radical concentrations are now known for the oxidation of hydrocarbons and aldehydes, the decomposition of acetaldehyde and of dimethylmercury, the polymerisation of a great many vinyl derivatives, the degradation of polymers, *e.g.*, poly(methyl methacrylate), and the interaction of bromotrichloromethane with olefins, such as *cyclo*hexene. This information at once makes it possible to calculate the velocity coefficients for the interaction of radicals with molecules, for example, in oxidations the rates at which peroxide radicals of the RO_2 interact with hydrocarbons and with retarders added to the system. Similarly, in polymerisation the rate of monomer addition to polymer radicals is known. Experiments of this kind have also demonstrated that a polymer radical grows at a speed almost independent of its size. In the more complicated case of copolymerisation of two monomers there are a minimum of ten elementary radical reactions. The velocity of each one may be calculated with a considerable degree of precision and the reaction mechanism may be said to be completely elucidated. By studying the copolymerisation system in which one of the reactants is fixed, it is possible to specify velocity coefficients of a given polymer radical with a great variety of other monomers, so shedding much light on the factors that govern radical reactivity.

The interaction of radicals provides many interesting problems. Although such reactions proceed without energy of activation, they are relatively inefficient since, except for the methyl radical, none so far discovered proceeds at a rate equal to the collision rate. Further, interactions are highly specific and may range over many orders of magnitude. This clearly demonstrates that chemical structure has in these cases a very great effect on the entropy terms in velocity coefficients. One even more surprising result is that dissimilar radicals interact much more quickly than would be expected from the separate reactivity of the radicals. Again, environment affects reactivity. If in polymerisation the viscosity of the system increases by the accumulation of polymer, radical–molecule interactions are unaffected but radical–radical interaction may be slowed up. This is due to immobilisation of the polymer radicals, whereas monomer can diffuse relatively easily to the polymer radical. This and many other surprising observations are the natural result of this new development. By such means there is the reasonable prospect in the near future that the mechanism of many chemical reactions involving radicals will be completely elucidated and set out in a satisfying quantitative fashion.

OBITUARY NOTICES.

THOMAS HILL EASTERFIELD.

1866—1949.

T. H. EASTERFIELD was born in Doncaster on March 4th, 1866, and died in Nelson, New Zealand, on March 1st, 1949. At an early age he entered the Yorkshire College (University of Leeds) and as early as 1883 published two papers, one chemical and one geological. Later he became a Senior Foundation Scholar of Clare College, Cambridge, and in 1886 was awarded a First Class in the Natural Science Tripos. He was a prominent long-distance runner, gaining his athletic blue. After graduation he worked in the University of Zurich and later under Emil Fischer at Würzburg, where he was later awarded a Ph.D. for a dissertation on citrazenic acid. He had returned to Cambridge in 1888 as a lecturer under the University Extension Movement, and he worked in the University Organic Chemistry Laboratory.

His varied experience, particularly in laboratory techniques, and his enthusiasm and lecturing to lay audiences, fitted him admirably for the post of Professor at the newly established University College at Wellington, New Zealand, to which he was elected in 1899, and it is notable that his inaugural lecture was entitled "Research as the Prime Factor in Scientific Education." Until 1908 his Chair also included that of Physics, but, in spite of the width of subjects upon which he was called to lecture, and the calls on his time for technical advice to local industries, and in spite of the primitive laboratories and conditions in scattered and unsuitable buildings, he immediately set about to conduct research on the chemistry of New Zealand flora, at that time a field relatively untouched. Within three years he had written eight papers on the subject, to be followed by many others until he resigned the Professorship in 1919, when he became director of the newly established Cawthron Institute at Nelson. In the meantime he had stimulated a large number of students into whom he had inculcated the research spirit; also he had exerted a profound influence on scientific matters in a number of local industries.

To this new post at Nelson he brought his characteristic enthusiasm, energy, and broad outlook, so that, when he retired in 1933 at the age of 66, it had become an institution favourably known throughout the Commonwealth. In his retirement he continued to devote his attention to research, his main interest being renal calculi and the reactions of permanganates in concentrated sulphuric and phosphoric acids.

Professor Easterfield took a leading part in the organisation and administration of scientific affairs in New Zealand. He was President of the Royal Society of New Zealand in 1921—22, and a Hector Medallist. The New Zealand Institute of Chemistry owed much to him in its formative years. For his services to science in New Zealand he was created a K.B.E. in 1938. He was a life member of the Royal Institute of Chemistry.

It may truly be said that through him Britain gave to New Zealand one of her most promising sons, and one who had a profound influence on the growth of more modern chemistry in that Dominion.

E. MARSDEN.

EDMUND GEORGE VINCENT PERCIVAL.

1907—1951.

EDMUND GEORGE VINCENT PERCIVAL, younger son of Albert Henry and Elizabeth Percival, was born at Hinckley in the county of Leicester on November 10th, 1907. He received his early education (1918—1925) at the King Edward VII Grammar School, Coalville, and afterwards became a student in the University of Birmingham where he read for an honours degree in Chemistry. These three years (1925—1928) showed him to be a brilliant scholar and his First Class Honours degree in 1928 was a true indication of his promise as a scientist. At this stage he decided to gain experience in several fields of research before choosing one in which to specialise, and in the autumn of 1928 he joined Dr. (now Professor) William Wardlaw's group at

Birmingham, working on the chemistry of inorganic co-ordination compounds. In 1929 he was awarded a Research Fellowship by the Canadian Pulp and Paper Association tenable at McGill University, where he worked in Professor Harold Hibbert's laboratory on physico-chemical problems concerning addition compounds of cellulose. Before returning to this country he visited numerous research centres in Canada and the United States, learning much and making many lasting friendships.

In the autumn of 1930 he returned to Birmingham in the capacity of senior research assistant to Professor Sir Norman Haworth. His interest in the chemistry of the carbohydrates, which was first awakened at Montreal, now developed rapidly and he soon decided to make this his main field of work. Three years later (1933) he was appointed to a lectureship in organic chemistry in the University of Edinburgh. Here he settled very happily, so much so indeed that it seems probable that he made no serious attempt to seek promotion by moving elsewhere. In 1934 he married Ethel Elizabeth Kempson whom he had first met in the chemistry laboratories at Birmingham, and in Edinburgh Mrs. Percival collaborated with her husband in much of his work on the sugars. She and their two children survive him. So great was Percival's interest in his research that he could not bear to be far away from the laboratories, and his home in Edinburgh was within a few minutes' walking distance of the Chemistry Department at King's Buildings. This nearness however brought with it additional advantages, since on the same site there were facilities for tennis and badminton and it was characteristic of Percival that when he was not hard at work he was usually to be found playing games with a similar intensity of purpose. Perhaps his only real regret over living in the north was occasioned by the lack of first-class cricket and the distance from Lord's.

He took a full part in the social and scientific life of the City and University. He became a member of the Faculty of Science and a Director of Studies. In 1948 he was promoted to a Readership in Chemistry in the University and in 1951 he was chosen to serve on the Senatus Academicus. His ability was such that awards came to him early—the Fellowship of the Royal Institute of Chemistry in 1936, the D.Sc. degree of Edinburgh in 1938, and the Fellowship of the Royal Society of Edinburgh in 1941. He gave freely of his services to various scientific societies and at the time of his death he was a member of Council of the Chemical Society and was serving on its Committee on Carbohydrate Nomenclature. For many years he was actively engaged in work for British Chemical Abstracts. He was interested also in the work of the Pharmaceutical Society and of the Institute of Brewing. He was one of the pioneers in the research work sponsored by the Scottish Seaweed Research Association on the chemistry of the marine algal polysaccharides, and he served with distinction from its inception on the Association's Chemical Advisory Committee. He was a member also of the Edinburgh and district committees of the Royal Institute of Chemistry and of the Society of Chemical Industry and for two years he acted as Chairman of the Edinburgh and South East Scotland section of the Institute. He rendered valuable service also as Local Representative of the Chemical Society. In 1948 when the annual general meeting of the Society of Chemical Industry took place in Edinburgh, and again in 1951 when he was Local Secretary for Section B of the British Association for the Advancement of Science, Percival's unselfish and unremitting work played a notable part in the success of the local arrangements for the meetings. He was a good lecturer and in consequence he received many invitations to visit other Universities and scientific societies, finding very special pleasure and satisfaction in those which involved considerable travelling. He was a most successful teacher, particularly for students of quick perception who could follow without difficulty his clear but somewhat rapidly developed exposition. Post-graduate students found in him an inspiring leader and director, friendly and approachable, supremely generous in all his actions, fertile in ideas and suggestions, and possessing an encyclopaedic memory for details. Especially characteristic of him were his kindliness, his deep sense of loyalty, and the capacity to see and appreciate the humorous side of everyday occurrences. Outside the laboratory he had many interests, prominent amongst which were his knowledge of painting, his passion for cricket, and the pleasure he took in holidays spent in the Border country near Kelso where he owned a small bungalow most delightfully situated within sight of the Cheviot hills. His students and colleagues will long remember the delightful hospitality accorded by Dr. and Mrs. Percival in their home in Mayfield Road. At the age of 43 he was at the height of his powers as a teacher and investigator, and his sudden death in Edinburgh on September 27th is a tragic loss to British Chemistry.

Percival's first research was carried out under Professor Wardlaw's direction at Birmingham (1928—1929) and was concerned with co-ordination compounds of cobalt (*J.*, 1929, 1317, 1505, 2628). Next came his work with Hibbert at Montreal where he studied the constitution of

soda-cellulose and showed that the adsorption of aluminium ions on cellulose was a base-exchange process (*J. Amer. Chem. Soc.*, 1930, **52**, 3257, 3448, 3995).

During the three years (1930—1933) which he spent in Sir Norman Haworth's laboratories Percival's attention was directed more and more to the structural side of carbohydrate chemistry, and he took part in the pioneering work of the Birmingham school on the molecular structure of the polysaccharides. Amongst the more important of the results he obtained at this period reference may be made to the evidence he provided by purely chemical means that the main structural feature of starch and glycogen is a chain of 1 : 4-linked glucopyranose residues. The method of approach was to subject the methylated polysaccharide to acetolysis, whereby a partially methylated disaccharide was obtained, which was then oxidised to the aldobionic acid and subjected to further methylation. Hydrolysis and identification of the products then showed that the maltose structure must be present in starch and glycogen. By similar methods the presence in xylan of chains of 1 : 4-linked xylopyranose units was demonstrated (*J.*, 1931, 1342, 2850; 1932, 2277). He applied the end-group method to inulin—a polysaccharide to the study of which he devoted much attention later—finding the proportion of non-reducing terminal fructofuranose residues to be 1 in 32, and to this period also belongs his important contribution to the work of the Birmingham school on the structure and synthesis of vitamin-C (*J.*, 1932, 2384; 1933, 1270, 1419).

After moving to Edinburgh in 1933 he continued his work in the carbohydrate group, and the numerous articles he published during the succeeding 18 years cover a wide variety of topics and are recognised as a major contribution to the development of sugar chemistry. The earlier work included studies of the addition compounds of carbohydrates with alkali-metal hydroxides, by which it was shown that the point of attachment of the inorganic and organic molecules could be determined (*J.*, 1934, 1160; 1935, 648; 1936, 1765; 1938, 1690). Reference compounds were needed for this work and Percival proceeded to study the structure of various monomethyl hexoses. He turned his attention also to the problem of the structure of the sugar osazones and by using the methylation method he obtained evidence that the osazones are not straight-chain compounds but possess a ring-structure, this being of the 2 : 6-type in glucosazone. During this work several new anhydro-osazones were isolated and studied (*J.*, 1935, 1398; 1936, 1770; 1937, 1320; 1938, 1384; 1940, 1479, 1511; 1941, 750; 1945, 783). Other activities in the monosaccharide field included the determination, by the application of conductivity measurements in boric acid solution, of the configuration of the groups attached to $C_{(1)}$ in derivatives of mannose and other sugars. In this way confirmation was obtained of the *trans*-arrangement of the hydroxyl groups on $C_{(1)}$ and $C_{(2)}$ in α-mannose derivatives (*J.*, 1937, 1920).

Much of Percival's most important work was, however, concerned with polysaccharides, and he had become an internationally recognised authority on the chemistry of plant mucilages and seaweed polysaccharides. He was one of the pioneers in the structural study of the carbohydrate components of the marine algae, with publications from 1936 onwards dealing with the structure of agar-agar. In the course of these difficult and complicated studies he demonstrated that 2 : 4 : 6-trimethyl D-galactose and derivatives of 3 : 6-anhydro-L-galactose are obtained on hydrolysis of methylated agar, but no detailed solution of the structural problem can yet be given (*J.*, 1937, 1615; 1939, 1844; 1942, 749). This was followed by investigations on the polysaccharides of *Chondrus crispus* (carragheen) and *Gigartina stellata*, in which some of the main structural outlines became manifest. In particular, evidence was obtained that the molecule contained a backbone of 1 : 3- or 1 : 6-linked galactopyranose residues similar to that present in many of the gums and naturally occurring galactans, but relatively rich in the case of carragheen in L-galactose residues (*J.*, 1943, 51; 1947, 1622; 1950, 1994).

These researches revealed the need for a more detailed knowledge of the properties of carbohydrate sulphate esters, and Percival published several papers (*J.*, 1938, 1585; 1940, 1475; 1941, 830; 1945, 119, 874; 1947, 1675; 1949, 1597) on the preparation of these compounds and their transformation into 3 : 6- and 5 : 6-anhydro-sugars on alkaline hydrolysis. Other work connected with seaweeds included the development of convenient methods of analysis for the various organic constituents, much of this being carried out in collaboration with the Scottish Seaweed Research Association (*J. Soc. Chem. Ind.*, 1948, **67**, 161, 420; 1950, **69**, 317). He was interested also in the chemistry of alginic acid, laminarin, and fucoidin (*J.*, 1950, 717, 827, 3494; 1951, 720), and in the interesting xylan present in *Rhodymenia palmata* which was found to differ markedly from other known xylans in containing both 1 : 4- and 1 : 3-linked xylan residues as main structural features (*Nature*, 1950, **166**, 787). But, even before this, Percival had become involved in the chemistry of xylose as the result of his extensive studies of the seed mucilages in the seeds of various members of the plantain family (*P. lanceolata*,

P. arenaria, *P. ovata*). These mucilages proved to be extraordinarily complex in structure, that from *P. arenaria* being composed of residues of galacturonic acid, arabinose, xylose, and galactose. Little is known as yet concerning the mode of attachment of the uronic acid portion but it is clear that in these mucilages the xylopyranose residues are linked in almost every possible way. For example, in the mucilage for *P. lanceolata* the following types of xylose residue were found to occur as building units: X1, 3X1, 4X1, $^{4}_{2}$X1, $^{4}_{3}$X1, and $^{3}_{4}X^{2}_{1}$ (*J.*, 1940, 1501; 1942, 58; 1949, 1600, 1608; 1950, 528).

In the hemicellulose group, studies were made of the complex nature of the polysaccharides present in Iceland moss (*J.*, 1943, 54), and Percival took part also in detailed investigations of the xylan from esparto, which showed that no arabinose residues are present and indicated a molecular structure containing some 75 1 : 4-linked xylose residues with one branch point (*J.*, 1950, 1289). A somewhat similar structure, but complicated by the presence of a terminal glucuronic acid residue, was recorded for the xylan from pear cell wall (*J.*, 1951, 1240).

Recent publications include papers on barley starch (*J.*, 1951, 2259) which was found to resemble other cereal starches in structure and in the proportion of the amylose and amylopectin components, and on the chemistry of wood starches (*J.*, 1951, 3489). Another main interest which Percival was developing vigorously up to the time of his death was the structure of the natural fructosans. Work on inulin (*J.*, 1950, 1297) demonstrated that glucose residues present to the extent of about 6%, were an integral part of the molecule, and this was followed by a detailed study of the fructosan from couch grass (*J.*, 1951, 1822). In this substance both 1 : 2- and 2 : 6-linked fructofuranose residues are present, and the structure appears to combine features present in inulin on the one hand and the natural levans on the other.

Both in his research work and in lecturing to advanced students Percival came to realise the need for an up-to-date text book covering the structural side of carhobydrate chemistry. His remedy was to write such an account himself and his " Structural Chemistry of the Carbohydrates " (1950), whilst remaining interesting and readable, is a marvel of compressed information. It has been received with acclamation by chemists in many countries of the world.

The work thus outlined was carried out within a period of 20 years, with the inevitable interruption of research facilities during the war. It is a notable achievement, all the more remarkable because it was never part of Percival's procedure to use complex apparatus or techniques. He tended rather to use simple and direct methods and to achieve his results by carefully thought-out plans of experimentation. He had a flair for recognising what was practicable, and his output of published work, amounting to some 70 papers, was made possible by this economy of effort, the remarkable speed and accuracy of his own practical work, the generous encouragement and inspiration he gave to his collaborators, and, above all, by the power and insight he displayed in devising methods for the solution of the problems he chose for investigation.

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